National Institute of Environmental Health Sciences

Environmental Factor

Your Online Source for NIEHS News

May 2013

NIEHS Spotlight

NIEHS delegation tours study sites in New Mexico

NIEHS and NTP Director Linda Birnbaum, Ph.D., toured NIEHS-funded study sites March 15-16 on a Native American reservation near Milan, N.M.

NIEHS sponsors international conference on flame retardants

NIEHS and NTP Director Linda Birnbaum, Ph.D., joined scientists and policy-makers April 7-10 at the Sixth International Symposium on Flame Retardants in San Francisco.

Training directors gather at NIEHS Video

Representatives of the 49 NIEHS-funded training grant programs met March 27-28 to learn about emerging trends in funding, workforce development, and diversity.

Norris outlines NIH Big Data initiative

NIH CIO Andrea Norris discussed efforts to upgrade information technology infrastructure for manage dramatically increasing amounts of data.

Folt named chancellor of UNC

Carol Folt, Ph.D., a member of the NIEHS-funded Dartmouth Superfund Research Program, is chancellor-elect at the University of North Carolina at Chapel Hill.

Science Notebook

The role of calcium signaling in immune function

Michael Cahalan, Ph.D., discussed the importance of calcium signaling in T cell function, and its potential as a therapeutic target for immune deficiency in humans.

NTP webinar informs Report on Carcinogens

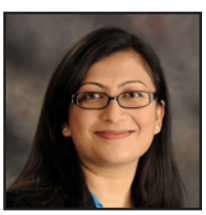
The NTP used a web-based format on April 11 to bring together scientific experts and members of the public to discuss pentachlorophenol (PCP) exposure and cancer.

Symposium features cutting-edge stem cell research

Stanford University's Gerald Crabtree, M.D., presented the keynote address at the NIEHS symposium on stem cells held April 11-12.

DNA methylation marker shows promise for detecting breast cancer risk

Jack Taylor, M.D., Ph.D., and Zongli Xu, Ph.D., led an NIEHS team that discovered DNA methylation was a better predictor of breast cancer risk than traditional methods.



NIEHS fellow begins career in clinical research

Darshini Trivedi, Ph.D., is now a clinical research scientist at Impact Pharmaceutical Services Inc. (IMPACT), thanks to networking, hard work, and perfect timing.

NIEHS Spotlight

National Institute of Environmental Health Sciences

International conference focuses on isocyanates and health

NIEHS co-sponsored a conference on isocyanates, a component of polyurethane products that may induce sensitization and asthma, April 3-4 in Potomac, Md.

Twenty years of research suggests asbestos regulations need updating Video

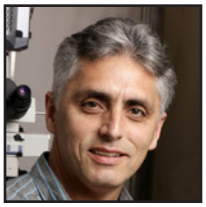
NIEHS Senior Medical Advisor Aubrey Miller, M.D., was a featured speaker at the annual international Asbestos Awareness Conference in Washington, D.C.

Hennig receives prestigious professorship at the University of Kentucky

Bernhard Hennig, Ph.D., has received a University Research Professorship for his work in understanding how nutrition affects health and disease.

EHS core center grantees gather in Seattle for annual meeting

The 2013 NIEHS Environmental Health Sciences (EHS) Core Centers meeting brought members from 20 cores centers to share their latest work in environmental health.



Yakel inspires future scientists

Jerrel Yakel, Ph.D., encouraged students to pursue science careers at the Tenth Annual Undergraduate Research Day April 18 at Saint Augustine's University.

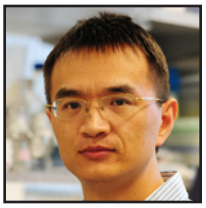
Science Notebook

Casey presents at workshop on stems cells in cardiotoxicity studies

Warren Casey, Ph.D., joined an international group of presenters to discuss how cultured heart cells may help scientists learn how chemicals affect the heart.

Farmland application of sewage sludge raises environmental justice concerns

People living near farmland treated with sewage sludge expressed concern, according to a study funded by the NIEHS Partnerships for Environmental Public Health.



Fatty acid metabolite inhibits tumor growth in mice

According to an NIEHS-funded UC Davis study, a product of omega-3 fatty acid metabolism fights cancer by removing the oxygen and nutrients that fuel tumor growth.

Brown bag lunch highlights careers in intellectual property and patent law

NIEHS fellows learned about career options in intellectual property and patent law from two former scientists that are currently working in the field as attorneys.

New protein mutated in neurodegenerative disease

Scott Williams, Ph.D., was part of an international team of scientists that identified a mutation in a protein that causes a rare form of neurodegenerative disease.

NIEHS Spotlight

NIEHS marks social media milestone

During the final week of March, NIEHS marked a social media milestone as the number of its Facebook likes exceeded 1,000 for the first time.

Clayton shines at area youth career fair

NIEHS biologist Natasha Clayton encouraged students to choose science as a profession at the Clarence E. Lightner YMCA Achievers Career Fair April 20 in Raleigh, N.C.

Inside the Institute

NIEHS ends weeklong Earth Day celebration with local highway adoption

NIEHS concluded its weeklong celebration of Earth Day April 26 by adopting the 1.2-mile stretch of Hopson Road between the main campus and Keystone building.

NIEHS celebrates and thanks administrative staff

Motivational speaker Earl Suttle, Ph.D., helped NIEHS administrative staff members enhance their careers at an event that honors their contributions to the Institute.

Science Notebook

NIEHS fellow transitions to career in biopharmaceuticals

Former NIEHS Laboratory of Molecular Genetics research fellow Rajesh Kasiviswanathan, Ph.D., has landed a new position at Fujifilm Diosynth Biotechnologies.

This month in EHP

This month's features in Environmental Health Perspectives examine the health impacts of Hurricane Sandy and environmental exposures in child care centers.

Upcoming distinguished lecture features Marie Davidian

Marie Davidian, Ph.D., a William Neal Reynolds Professor in the Statistics Department at NCSU, will discuss the role of statistics in personalized medicine.

Extramural Research

Extramural papers of the month

- Prenatal DDT exposure associated with high blood pressure in adults
- Blocking glucocorticoid receptor prevents arsenic-induced birth defects
- Community beliefs regarding dioxin exposure pathways
- BPA exposure in the NICU

Intramural Research

Intramural papers of the month

- A novel mechanism underlies glucocorticoid resistance
- COX-2 involved in the development and worsening of asthma symptoms
- Early life socioeconomic factors influence the development of rheumatoid arthritis
- Specific DNA polymerase active site residue may influence a cell's mutagenic response to oxidative stress

Calendar of Upcoming Events

- **May 1**, in Keystone 3003, 12:00-1:00 p.m. — “Prenatal Exposure to Persistent Pollutants in a 20 Year Old Danish Cohort: Results and Future Direction,” by Thorhallur Halldorsson, Ph.D.
- **May 2**, in Rall F-193, 11:00 a.m.-12:00 p.m. — Laboratory of Toxicology and Pharmacology hosted presentation on “Autism Spectrum Disorders and Shank3 Disruption in Mice,” by William Wetsel, Ph.D.
- **May 3**, in Rodbell A, 11:00 a.m.-12:00 p.m. — Laboratory of Reproductive and Developmental Toxicology hosted seminar on “Phenobarbital Indirectly Activates the Constitutive Active Androstane Receptor (CAR) by Inhibition of Epidermal Growth Factor Receptor Signaling and the Function of Transactivation Domains of Estrogen Receptor A,” by Shingo Mutoh, Ph.D., and Yukitomo Arao, Ph.D.
- **May 8**, in Rodbell Auditorium, 11:00 a.m.-12:00 p.m. — Distinguished Lecture Series featuring Marie Davidian, Ph.D., discussing “The Right Treatment for the Right Patient (at the Right Time)”
- **May 14**, in Rodbell Auditorium, 8:30 a.m.-5:00 p.m. — National Advisory Environmental Health Sciences Council
- **May 21**, in Rall F-193, 12:30-2:00 p.m. — “DNA Repair Videoconference: Human DNA Repair Disorders, a Historical Perspective,” by Alessandro Vindigni, Ph.D.
- **May 21 (offsite event)**, in Room C111A, at U.S. Environmental Protection Agency in Research Triangle Park, N.C., 8:00 a.m.-4:00 p.m. — Genetics and Environmental Mutagenesis Society (GEMS) Spring Symposium, “Mechanisms of Environmental Carcinogenesis”
- View More Events: NIEHS Public Calendar

NIEHS Spotlight

NIEHS delegation tours study sites in New Mexico

NIEHS and NTP Director Linda Birnbaum, Ph.D., toured NIEHS-funded study sites March 15-16 on a Native American reservation, Laguna Pueblo, and at an abandoned uranium mill near Milan, N.M. She and Mary Gant, NIEHS Program Analyst, were the guests of Johnnye Lewis, Ph.D., professor and director of the Community Environmental Health Program at the University of New Mexico (UNM).

Lewis has been involved in health projects with Native Americans in northwest New Mexico since 1991. She currently has funding from NIEHS to study the impact of chronic uranium exposure on kidney function, and from the Agency for Toxic Substances and Disease Registry to study the effects of uranium exposure on pregnancies, birth outcomes, and development of children.

Birnbaum listened to community leaders, such as Laguna guide Larry Lente, right, a thirty-year Marine veteran and former mineworker. (Photo courtesy of Mary Gant)

In conversations with community representatives, including the vice president of the Navajo Nation, Birnbaum briefly described the NIEHS vision, mission, current research activities, and the new five-year strategic plan. She emphasized the importance of continuing relationships with Native American communities as one of the most important elements of the plan.

As an example of ongoing interest at NIEHS in Native American environmental health issues, Birnbaum pointed to the December 2012 webinar on "Environmental Justice: A Native American Perspective," which attracted more participants than any other NIEHS webinar. "Protecting our health means protecting our environment," she said. "Clean air, clean water, and clean land are essential to preventing disease."

Unlike community meetings in urban areas, a meeting on the reservation took place on a gravel lot adjacent to the Northeast Church Rock Mine in the Red Water Pond Road community. (Photo courtesy of Mary Gant)

Birnbaum and Gant observed reclamation efforts intended to reduce exposures for residents. They also heard from community members about high concentrations of uranium in surface water immediately downstream.

Other pollutants detected in the area include arsenic, barium, chromium, cobalt, copper, lead, manganese, vanadium, selenium, and zinc. The Laguna people have asked the U.S. Environmental Protection Agency to declare the area a Superfund site.

The NIEHS delegation spent its final day, March 18, at UNM with NIEHS-funded researchers discussing current projects.

Earlier activities supported by NIEHS include uranium education at the Navajo Nation Dine College, and the Dine Network for Environmental Health study that the Eastern Navajo Health Board requested, because of concern over exposure to uranium in drinking water. Its goal was to build community research capacity and study community health.

The former Jackpile-Paguate Uranium Mine on the Laguna Pueblo, 40 miles west of Albuquerque, shows the results of typical remediation efforts, which consisted of covering mine waste and contouring to reduce erosion. However, runoff from the site pollutes water downstream. (Photo courtesy of Mary Gant)

Return to Table of Contents

NIEHS sponsors international conference on flame retardants

By Sara Mishamandani

Scientists and policymakers from around the globe met to discuss current research on the potential health effects of flame retardants April 7-10 at the Sixth International Symposium on Flame Retardants in San Francisco. NIEHS and NTP Director Linda Birnbaum, Ph.D., is well known for her own research in this area. NIEHS, along with other sponsors, provided funding for the meeting.

Flame retardants are found in many consumer products, such as baby bedding, foam cushions, carpet padding, clothing, and electronics. The compounds are everywhere in the environment, and researchers are concerned that exposure to these chemicals, at an early age, may lead to a range of detrimental health effects later in life, either by increasing susceptibility to disease or by initiating disease processes.

Birnbaum presented an overview of the prevalence and toxicity of flame retardants, during a plenary lecture. She stressed the need to move to research that is predictive rather than reactive, with knowledge of health effects, before chemicals are added to consumer products. If alternative chemicals are needed, Birnbaum said we need to avoid regrettable alternatives that are just as harmful as the originals. She also emphasized that more attention should be paid to the need for flame retardants in products.

Birnbaum described methods to measure compounds and identify their toxicity. She said the chemically activated luciferase gene expression (CALUX) cell bioassay is an excellent example of an innovative tool to improve understanding of environmental exposures. CALUX is a rapid assay used to detect and quantify dioxin and dioxin-like chemicals that was developed through the University of California (UC), Davis, Superfund Research Program (SRP).

Superfund scientists lead the way

"The conference brought together a small community from around the world interested in the same topic," said Candace Bever, Ph.D., from the UC Davis SRP. "Reports of flame retardants in environmental or human samples were presented from 16 countries on five different continents."

NIEHS SRP grantees Heather Stapleton, Ph.D., from Duke University, and Thomas Webster, D.Sc., from Boston University, served as session chairs and members of the national organizing committee. Stapleton also gave a plenary talk.

"Almost half of the conference presentations referenced work by Stapleton or Webster, for comparison or justification of research," said Bever. "The numerous citations and acknowledgements demonstrate their contributions to this field of science and the relevance of SRP-funded research."

Bever, right, and Myrto Petreas, Ph.D., left, an environmental scientist at the California Department of Toxic Substances Control, were lead researchers on the NIH conference funding award. The award funded student travel and session support during the conference. (Photo courtesy of Candace Bever, UC Davis SRP)

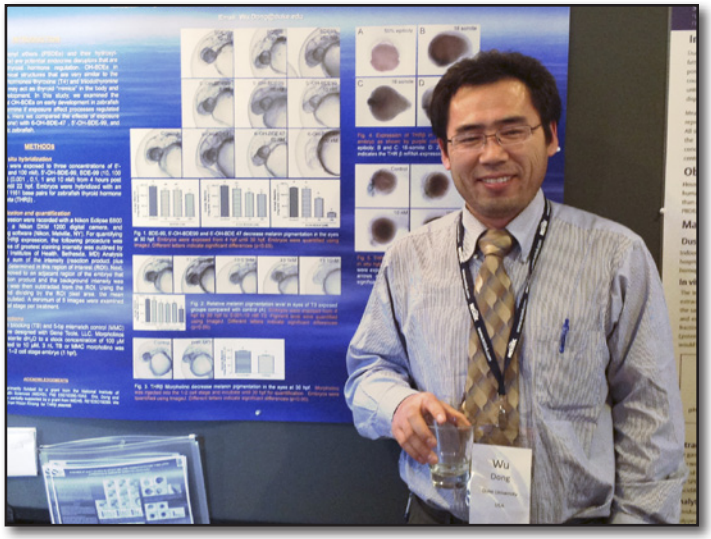
Birnbaum, a leading authority in the field, presented a talk during a plenary session at the conference. (Photo courtesy of Candace Bever, UC Davis SRP)

SRP investigators and session chairs Webster and Stapleton. (Photo courtesy of Candace Bever, UC Davis SRP)

An emphasis on multidisciplinary research

"During the conference, it was great to have all of the attendees in the fields of chemistry, biology, industry, and policy in the same room," said Bever. "Chemists need biologists to explain the issues surrounding health effects, biologists need chemists to explain how flame retardants travel through the environment, and everyone has to work together to inform policy."

Because there were no concurrent presentations, all researchers from multiple disciplines participated in all sessions. The progression of talks began with scientists describing where they are finding flame retardants, movement of flame retardants in the environment, how these chemicals are getting into humans and affecting them, and ended with a discussion on public policies that address flame retardants in consumer products and the environment.



SRP trainee Wu Dong, Ph.D., presented a poster on the health effects of specific flame retardant chemicals. (Photo courtesy of Candace Bever, UC Davis SRP)

Conference presenters stressed the emerging need to understand the fate and transport of flame retardant chemicals in the natural environment and human bodies. They agreed that public policy has focused on flame retardants in building and consumer products in the past, but acknowledged that many of these products are ending up in landfills, releasing flame retardant chemicals into the environment.

Abstracts from both oral and poster presentations are available on the meeting website.

(Sara Mishamandani is a research and communication specialist for MDB Inc., a contractor for the NIEHS Superfund Research Program and Division of Extramural Research and Training.)

Return to Table of Contents

Training directors gather at NIEHS

By Eddy Ball

Representatives of the 49 NIEHS-funded training grant programs met March 27-28 to learn about emerging trends in funding, workforce development, and diversity. The grants, awarded under the Ruth L. Kirschstein National Research Service Awards (NRSA), support training programs for graduate students and postdoctoral trainees. Also invited to attend were the directors of the three NIEHS short-term summer research programs for medical students, and the four directors of the short-term summer research programs for high school and undergraduate students.

Following a welcome from NIEHS Program Administrator Carol Shreffler, Ph.D., NIEHS and NTP Director Linda Birnbaum, Ph.D., addressed the critical role of training in the NIEHS strategic plan, developments in the budget process, and her one-NIEHS vision for advancing the environmental sciences.

Birnbaum was candid about the effects of budget cuts on grants. "The pay lines are going to drop," she said. But Birnbaum was also eager to assure the training directors that the burden would fall evenly across all the programs NIEHS supports. "Intramural programs are also taking a hit," she added.

Responding to Birnbaum's enthusiasm for training successes and the deep commitment of NIEHS to training programs, several attendees, afterward, described her presentation as upbeat and reassuring.

Linked video:

Watch the award-winning "These Are the Days of Our Lives… As Toxicologists" video that Birnbaum recognized during her presentation (06:37)

(Launches in new window)

Download Media Player: Flash

New initiatives in training and diversity

Directors and representatives of new training programs reported on their operations and curriculum design, as well as efforts to enrich their programs with existing resources at their institutions. Each of the programs includes a proactive agenda for increasing the diversity of participants, and implementing innovative approaches to better prepare trainees for a changing job market.

These themes were developed even further in videocasts featuring representatives of NIH advisory committees to the director (ACDs) on the issues of biomedical research workforce development and diversity in the biomedical workforce (see text box). They also emerged in discussions of evaluation and future directions, later in the meeting.

Funding decisions — a view from the other side

In her report, NIEHS Division of Extramural Research and Training (DERT) Director Gwen Collman, Ph.D., quickly established an atmosphere of trust and shared interests, by helping attendees understand how DERT scientific administrators make their decisions. She presented a candid description of the difficult process of reviewing grant applications and setting funding priorities.

"We are so broad," Collman explained, pointing to the range of programs that complicates decision-making by DERT staff. "We spend a lot of time arguing about these choices in-house," she said.

In search of a fair and just way to recommend awards, and make the greatest number of awards with available funds, Collman said her staff must balance potentially high-impact proposals with consideration for ongoing programs that are making steady, if not headlines-grabbing, progress toward their objectives.

During her talk, Birnbaum referred to the centuries of expertise about training in the environmental health sciences, represented in the collective experiences of people at the meeting. (Photo courtesy of Steve McCaw)

University of Pennsylvania representative Trevor Penning, Ph.D., center, who described the good fit of the NIEHS program into the pipeline of training at his institution, continued the discussion with colleagues during a break in the meeting. (Photo courtesy of Steve McCaw)

Rebecca Fry, Ph.D., center, of the University of North Carolina at Chapel Hill, also took advantage of the break to catch up with colleagues from other programs — David Christiani, M.D., left, of Harvard University, and Daniel Liebler, Ph.D., of Vanderbilt University. (Photo courtesy of Steve McCaw)

In an effort to maximize funds for awards and reduce travel expense, she added, "We're trying to think about the future in terms of virtual collaborations."

Defining and measuring success

On day two, DERT Program Evaluation Branch Chief Christie Drew, Ph.D., discussed her staff's progress with CareerTrac, a structured database tool for following long-term training outcomes. As Shreffler said in her introduction of Drew, "We really don't know a lot about where trainees are going."

To address that uncertainty, Drew outlined a pilot system, established last year, to describe trainee outcomes, and offer training programs a measure of accountability, with a main focus on the past ten years. With nearly 7,000 NIEHS trainees loaded into the system, Drew's team is continuing to solicit input for refining endpoints, such as scientific and technical emphasis codes, and employment sector and status classifications, with the goal of having data entry completed by September.

"I think for the first time, we're really going to get some answers," Drew concluded.

Attendees devoted the remaining half day of their meeting to discussions of the NIEHS training and workforce development strategic plan, in workgroups moderated by Shreffler and NIEHS Program Administrator Michael Humble, Ph.D. Program representatives considered undergraduate curriculum

Workforce training and support

NIH Director of Policy and Liaison Activities Henry Khachaturian, Ph.D., reviewed statistics about the current biomedical research workforce, before presenting ACD recommendations to advance NIH support for a future sustainable biomedical infrastructure.

Khachaturian pointed to the large upsurge in biomedical Ph.D.s, and long training times that complicate launching a traditional research career. Comparatively, low starting salaries, he said, contribute to making the biomedical research career less attractive, and current programs inadequately prepare trainees for anything other than an academic research career.

The recommendations address issues with graduate students, physician scientists, and staff scientists, but are especially pointed in terms of the postdoctoral experience, where training needs to be enhanced to better match available off-the-bench careers, where nearly one-third or more of trainees end up working.

Implementation of ACD recommendations, including an increase in trainee stipends and benefits, is progressing, Khachaturian explained, but the exact details and timing will still be undergoing review and clearance following the April 22 deadline for public comment.

Workforce diversity

NIH Extramural Program Scientific Workforce Diversity Specialist Lisa Evans, J.D., opened her presentation with two pie charts that painted a picture truly worth the proverbial thousand words. While the percentage of white principal investigators (PIs) receiving NIH research project grants (RPGs) is almost equal to the percentage of whites in the population, African-Americans, with 12.6 percent of the population, represent just 1.1 percent of PIs with RPGs. Latinos fare a little better, 16.3 versus 3.5 percent, while Native Americans, with 0.9 percent of the population, represent but a sliver of the RPG pie.

With recommendations from its working group, the ACD for workforce diversity has identified four interrelated approaches for addressing these glaring disparities, by increasing support for students through special awards to expand mentorship, and ensuring fairness in peer review through implicit bias and diversity awareness training. The recommendations call for recruitment of a permanent chief officer for scientific workforce diversity, to coordinate NIH initiatives and oversee rigorous prospective evaluation of existing NIH programs.

development and pipeline to graduate training, innovations in training at the graduate and postdoctoral level, curriculum and development research training programs in emerging scientific areas, and peer review for innovative programs.

Collman described what goes on behind the scenes when choosing grant applications. She assured her listeners, "I am really invested in your future." (Photo courtesy of Steve McCaw)

Drew, shown at an earlier talk about CareerTrac, considered comments about tenure track designation as an endpoint for training evaluation. As this data entry item and several others demonstrated, classifying outcomes is not as easy as it may seem at first. (Photo courtesy of Steve McCaw)

New program representatives gathered as a panel to discuss new directions in training and tracking progress. Shown, left to right, are Christopher Simpson, Ph.D., of the University of Washington; Lauren Aleksunes, Pharm.D., Ph.D., of Rutgers University, who is also an Outstanding New Environmental Scientist awardee; and Marianne Wessling-Resnick, Ph.D., of Harvard University. (Photo courtesy of Steve McCaw)

Among the training directors with questions and comments about new directions in workforce development was Gary Miller, Ph.D., of Emory University. (Photo courtesy of Steve McCaw)

Thomas Gasiewicz, Ph.D., of the University of Rochester, joked about the trainee film from his program that received an award from the Society of Toxicology (SOT). "It was the only video in the competition," he said. (Photo courtesy of Steve McCaw)

During his review of a discussion about pipeline issues, Humble reflected on changes in training emphasis that are expected from ACD workforce recommendations. "It's really a big unknown," he said. (Photo courtesy of Steve McCaw)

Shreffler, who had the first word at the meeting, also closed the gathering with a hearty expression of her appreciation for attendees' input during the breakout sessions. (Photo courtesy of Steve McCaw)

Return to Table of Contents

Norris outlines NIH Big Data initiative

By Richard Sloane

New efforts are underway to manage the huge amounts of scientific data being produced by researchers throughout the National Institutes of Health, according to NIH Chief Information Officer Andrea Norris, who gave a talk March 29 at NIEHS about the NIH Big Data to Knowledge (BD2K) initiative.

Norris explained that BD2K aims to create improved data and software sharing policies, catalogs of research data, and the development of data and metadata quality standards. She said she expects to see a significant long-term investment by NIH for accelerated software development and enhanced training through new biomedical big data centers of excellence.

According to Norris, the BD2K initiative would create an advanced computing environment called InfrastructurePlus, which would ultimately modernize the NIH network to meet data handling requirements through a much more robust network. Ideally, InfrastructurePlus would advance high-performance computing, and agile hosting and storage approaches for different data domains.

Big Data means very big numbers

Big Data is measured in terabytes, or trillions of bytes, and petabytes, or quadrillions of bytes, but according to some experts, within a decade, even those numbers may be inadequate.

According to estimates by Eric Schmidt, Google's former chief executive officer, the world creates 5 exabytes, or quintillions of bytes, of data every two days — roughly the same amount of data created between the dawn of civilization and 2003.

It's estimated that NIH generates 4 petabytes of data each day.

"Fundamental change in the way we gather and use massive amounts of data is overdue," said Norris. The aging NIH computer network currently runs at 80 to 90 percent capacity during peak utilization, far higher than the desirable 30 to 40 percent. According to Norris, meeting the challenge of managing growing amounts of data (see text box) involves more sophisticated technology, a dedicated research network, better harmonization tools, and even cultural evolution.

Issues and opportunities

"Big data is changing dramatically how we do science," Norris said. "Accessing these massive pools of data will most likely require new skill sets by scientists."

More scientists are increasingly using pooled data, instead of working with only their own. In many circles of science, teams of researchers are leveraging large, and even massive, amounts of data (see story).

This new kind of shared data approach challenges the culture of scientific research, Norris said, because it will require the community to recognize the value of generating good data, and allowing access to that data. The research culture at NIH will need to change, to respond effectively to new developments in an ever-changing technology landscape.

Many questions remain

Bioinformatics, genetics, and genomics studies produce and consume massive amounts of data. Yet many questions arise. How will this data be stored? How will it be accessed? Who will be in control? What are the hardware and software challenges to facilitate big data management? How will data be shared? How can data quality be assured and adaptable to the needs of science? How long should data be stored?

"We are learning," Norris explained. "In five years we'll look back and realize how naïve we were on some of these approaches. Whatever we're doing today, we expect to adapt, mature, and evolve over time."

(Richard Sloane is an employee services specialist with the NIEHS Office of Management.)

Birnbaum listened to community leaders, such as Laguna guide Larry Lente, right, a thirty-year Marine veteran and former mineworker. (Photo courtesy of Mary Gant)

Employees from every division of NIEHS attended Norris' presentation, including NIH Human Resources Specialist Angela Davis, left, and NIEHS Employee Services Manager Ed Kang. (Photo courtesy of Steve McCaw)

Also part of the audience were, right to left, NTP Deputy Division Director for Policy Mary Wolfe, Ph.D.; NTP Deputy Director of the Office of Health Assessment and Translation Andrew Rooney Ph.D.; and NIEHS Informationist Stephanie Holmgren. (Photo courtesy of Steve McCaw)

Despite the seriousness of the current situation, Norris could also speak to the lighter side of NIH culture. Shown above enjoying the comic relief, left to right, were Kang; NIEHS Project Officer Beth Ragan; Program Administrator David Balshaw, Ph.D.; Health Science Administrator Symma Finn, Ph.D.; and Grants Management Specialist Molly Puente, Ph.D. (Photo courtesy of Steve McCaw)

Senior Associate Scientist Dmitry Gordenin, Ph.D., was one of many researchers who expressed their interest in better tools for harnessing big data, and open access to government-funded research. (Photo courtesy of Steve McCaw)

Birnbaum joined Norris during the question and answer session. Birnbaum described effective data management as critical for advancing strategic plan initiatives. (Photo courtesy of Steve McCaw)

Return to Table of Contents

Folt named chancellor of UNC

On April 12, the University of North Carolina at Chapel Hill (UNC) elected Carol Folt, Ph.D., to be its 11th chancellor. Folt is interim president of Dartmouth College and a member of the NIEHS-funded Dartmouth Superfund Research Program. She will assume her new role July 1, and will be the first woman to lead the university. A press release about Folt's appointment is available through the UNC website.

Carol Folt, Ph.D., is chancellor-elect at UNC. (Photo courtesy of Dan Sears, UNC)

Folt's areas of expertise include ecotoxicology, health-environment interactions, and science education, with a research focus on metal toxicity and the effects of dietary mercury and arsenic on aquatic life and human health. Folt and her colleagues developed new technologies to assess mercury environmental exposure and its effects, and have also conducted crosscutting research on global climate change, as well as chemical signaling, restoration, and conservation of Atlantic salmon.

"It has been a great pleasure to have worked with Carol over the years as part of the Superfund Research Program (SRP)," said NIEHS SRP Director Bill Suk, Ph.D. "I am very excited that she will be the chancellor of UNC Chapel Hill. She will be wonderful in the position."

She is also the associate director and a co-investigator of the NIEHS and U.S. Environmental Protection Agency-funded Children's Environmental Health and Disease Prevention Research Center at Dartmouth College.

"Over the past three decades, Carol Folt has accumulated a wealth of academic and leadership experience at one of the top 10 universities in America," said Thomas Ross, president of the 17-campus University of North Carolina system. "At each step along the way, she has proven herself to be an engaged and effective leader who promotes openness and collaboration, strategic thinking and creative problem-solving, and an unwavering commitment to academic excellence and student success. She has also earned a reputation for great integrity, sound judgment, and the ability to face tough and complex challenges head-on."

A faculty member at Dartmouth since 1983, Folt was named provost in May 2010 and later appointed Dartmouth's interim president in July 2012. An internationally recognized environmental scientist and award-winning teacher, she has served the college in a series of senior academic and administrative roles since 2001.

Return to Table of Contents

International conference focuses on isocyanates and health

By Paula Whitacre

From foam insulation to sealants, mattresses to bowling balls, isocyanates are everywhere as a component of polyurethane products. Although it is known that exposure to isocyanates can induce sensitization and asthma in workers who handle them unsafely, many questions still remain. Are there other health effects, such as certain cancers, related to isocyanate exposure? How can isocyanate occupational exposures be measured and reduced,

especially among workers in less-regulated, often small-scale enterprises in the United States and around the world? Can consumers also experience health effects from exposures to various household and do-it-yourself products?

An international conference, Isocyanates and Health: Past, Present, and Future, brought together scientists, regulators, worker representatives, industry representatives, clinicians, and others to answer these and other questions April 3-4 in Potomac, Md. NIEHS, along with other U.S., Canadian, and European professional societies, government agencies, and companies, co-sponsored the conference.

Aubrey Miller, M.D., NIEHS senior medical advisor, discussed NIEHS-supported research and collaborations. His team also hosted an NIEHS exhibit during the conference poster sessions.

"The purpose of the conference was to identify and discuss the latest knowledge and best evidence, and to identify research gaps," said James Lockey, M.D., of the University of Cincinnati College of Medicine and scientific chair of the conference. "It was important that we include all the stakeholders at the table." According to Lockey and several other attendees, it was the first international multistakeholder conference to focus on isocyanates since 2001.

Lockey, scientific chair of the Isocyanates and Health conference, opened the meeting by reviewing the goals with participants. (Photo courtesy of Halvor Erikstein)

Feng provided an overview of the past, present, and future of isocyanates. (Photo courtesy of Halvor Erikstein)

Polyurethane: promise and peril

As ubiquitous as polyurethane is now, it was invented in 1937 by the German chemist Otto Bayer. It soon became widely used, because of its versatility and utility, according to keynote speaker Sharon Feng, Ph.D., of the University of Chicago. Different isocyanate compounds, most commonly toluene diisocyanate (TDI) and methylene bisphenyl isocyanate (MDI), are used, depending on the desired qualities of the final product.

Multistakeholder participation in the conference enriched the discussion. Andrew Comai, standing, an industrial hygienist with the UAW International Union Health and Safety Department, gave a report from a breakout session to the plenary. (Photo courtesy of Helvor Erickstein)

From a health and safety perspective, Feng emphasized, "Isocyanates are reactive chemicals that need to be handled in a safe manner." How to handle them safely under various conditions, how to assess and communicate the risks, and how to find answers to the many unknowns about exposure, biomarkers, and other issues ran through the rest of the conference.

Over two days, the conference included plenary overviews and discussions, along with oral and poster presentations. The specific research findings covered six thematic areas:

- Worker and consumer exposure issues
- Toxicity testing, animal models, and biomarkers
- Human cancer risk
- Environmental exposure and monitoring
- Respiratory epidemiology and disease
- Occupational health surveillance and management

The diverse ways that participants interact with isocyanates in their work, both indirectly or directly, enriched the discussions concerning research gaps and future priorities. At the end of the conference's second day, chairs of the thematic areas reported out draft lists of research priorities, based on the discussions and a pre-conference survey. The meeting summary and research priorities will be published in the Journal of Occupational and Environmental Medicine.

At a follow-up workshop, Miller discussed NIEHS models of research collaboration. (Photo courtesy of Paula Whitacre)

From left to right, Miller; Pertti (Bert) Hakkinen, Ph.D., of the National Library of Medicine; and Gary Ellison, Ph.D., of the National Cancer Institute, helped brainstorm ideas for moving forward and leveraging resources related to isocyanates research. (Photo courtesy of Paula Whitacre)

Moving forward

A workshop for agency representatives, chairs of the thematic areas, and the conference planning committee immediately followed the larger two-day conference. According to facilitator Andrew Maier, Ph.D., of Toxicology Excellence for Risk Assessment (TERA), the workshop was designed to share information on different models of collaboration and leveraging of resources to enhance the impact of research funding on isocyanates and health.

Representatives from several organizations involved in collaborations and partnerships, including NIEHS, explained their models for possible use or expansion related to isocyanates. Miller said, the NIEHS mission and priority areas encompass isocyanate activity and research, including the Worker Education and Training Program, the National Toxicology Program, and funded research focusing on neurotoxicity and the development of biomarkers of isocyanate exposure.

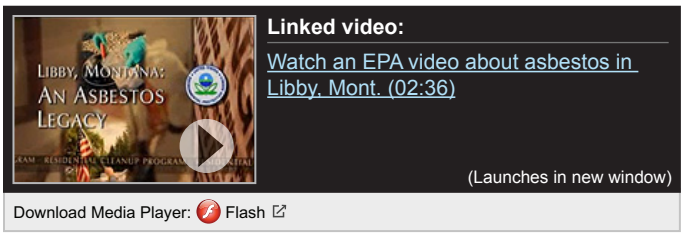
(Paula Whitacre is a contract writer with the NIEHS office in Bethesda, Md.)

Return to Table of Contents

Twenty years of research suggests asbestos regulations need updating

By Pamela Kidron

Asbestos regulations were last updated in the mid-1980s, and more than 20 years of health research suggests it's time to update those regulations again, said NIEHS Senior Medical Advisor Aubrey Miller, M.D., during a March 23 keynote speech at the annual international Asbestos Awareness Conference in Washington, D.C. New research shows that much lower exposures to asbestos can cause disease, Miller continued.



Exposure to asbestos is dangerous for mining and industry workers, and it is also a risk for communities exposed to it through the environment. Examples of asbestos in the environment include asbestos dust brought into households by workers, as well as asbestos-contaminated products and gravels used for road paving.

This issue attracted wide attention in 1999, when a newspaper article reported 192 people dead and 375 sick from asbestos-related diseases in Libby, Mont., even though the vermiculite mine there had closed a decade earlier. The vermiculite from the mine in Libby was contaminated with naturally-occurring asbestos.

At the conference, Miller used Libby as a case study, to show the assembled asbestos patients, caregivers, and medical experts how existing asbestos regulations could be improved to protect workers and communities. Miller said that asbestos health standards have not kept up with science, and that new realities such as the risks from environmental exposures now confront the public.

According to Miller, Libby, Mont. raised awareness of the potential harm from non-occupational exposure to asbestos. (Photo courtesy of Steve McCaw)

Remembering the worst public health incident in EPA history

The Libby disaster unearthed gaps in asbestos regulations, Miller explained. Laws were primarily aimed at protecting mine workers, not communities that had been put at risk by household contact with workers or their clothes, from living near a site where asbestos was mined, or from being exposed to asbestos-contaminated products, such as vermiculite insulation used in Libby and in millions of residences throughout the United States.

"How could a disaster like this [in Libby] have happened, when we already knew about the danger of asbestos for almost a hundred years?" asked Miller, who was with the U.S. Environmental Protection Agency (EPA) at the time, coordinating multi-agency emergency responses to public health problems. "These low-dose exposures

[in the environment] weren't supposed to make people sick. Only those high-exposure workers were getting sick. Right? That's what our laws were meant to do — to keep those high-risk workers safe."

Miller and the EPA team screened the town for health problems, and found that 18-20 percent of the adult population had asbestos-related disease, and that most of these cases were not related to mining exposures.

Researchers also found that the current methods being used to identify hazardous products, materials, or soils contaminated with asbestos, were not effective in protecting workers or the public from dangerous asbestos exposures. Current law permits the use of up to one percent of asbestos in materials that readily release asbestos fibers when disturbed. Yet materials containing asbestos, well below one percent, can be very dangerous.

Additionally, current standards do not regulate other dangerous, asbestos-like mineral fibers, such as erionite, a potent carcinogen. "Erionite-contaminated gravels were used in Dunn [County], N.D., to pave more than 300 miles of roads, including 32 miles of school-bus routes. EPA testing of school buses driving on the gravel roads found elevated air levels of erionite, similar to towns in Turkey with high rates of mesothelioma," noted Miller.

Challenging perceptions about asbestos

People do not understand the seriousness of exposure to asbestos, and many mistakenly think that asbestos has been banned and is no longer a problem, said Miller. Yet asbestos continues to be used in home and transportation products. It is still being imported, there is no ban on exporting it, and deaths from malignant mesothelioma, a cancer primarily associated with asbestos exposure, are still on the rise.

Miller stressed the need to update asbestos regulations, as soon as possible. "We need to push for lower exposure levels, to fund fundamental research to identify what is toxic about these materials, and to address materials, such as erionite, currently not regulated as asbestos," he told the attendees. "We also need to push for modernizing techniques for sampling and analysis, and to test consumer products potentially contaminated with asbestos."

(Pamela Kidron is a contract writer with the NIEHS office in Bethesda, Md.)

Return to Table of Contents

U.S. surgeon general warns about dangers of asbestos

U.S. Surgeon General Regina Benjamin, M.D., has urged Americans to learn about the dangers of asbestos exposure. The warning came in an April 1 statement she issued in support of National Asbestos Awareness Week.

The Asbestos Disease Awareness Organization (ADAO) applauded the surgeon general's statement, and took the opportunity, once again, to urge Congress to ban asbestos and stop asbestos imports.

Benjamin stressed that preventing the damage caused by asbestos was key to keeping Americans healthy and safe in their homes. "Together, we can prevent the dangers associated with asbestos," she said in her statement.

ADAO has been working with Congress and the White House since 2004, to prevent asbestos exposure. Responding to the surgeon general's statement, ADAO co-founder and president Linda Reinstein noted that there is consensus among the EPA, National Institute for Occupational Safety and Health, National Toxicology Program, World Health Organization, International Labour Organization, and International Agency for Research on Cancer that asbestos is a carcinogen and that there is no safe level of exposure.

Hennig receives prestigious professorship at the University of Kentucky

By Carol Kelly

Bernhard Hennig, Ph.D., director of the University of Kentucky (UK) Superfund Research Center (SRC) and professor of nutrition and toxicology in the College of Agriculture, is the recipient of a University Research Professorship. These professorships recognize outstanding UK researchers who have established a national reputation for sustained contributions to their field, and carry an award of $40,000.

Hennig's distinguished research program is broadly focused on understanding mechanisms underlying the positive effects of selected nutrients on human health. Although Hennig has always been interested in how nutrition can affect health and disease, his work with the SRC has driven discoveries about how nutritional sciences and toxicology can overlap or be interrelated scientific disciplines.

Hennig, left, receives a University Research Professorship award plaque from Eli Capilouto, D.M.D., Sc.D., president of the University of Kentucky. (Photo courtesy of Bernhard Hennig)

"The concept that nutrition can modulate how people respond to disease risks associated with exposures to Superfund pollutants is fascinating," said Hennig.

Blending nutritional and toxicological environmental research

Hennig's research provides evidence that people may reduce their risk to environmental pollutant exposures through healthy nutrition. He contends the research supports a paradigm shift where nutrition or dietary health is a critical player in overall vulnerability to environmental stressors.

Hennig's research group is well known for a finding that suggests the type of fat we eat can alter how our bodies respond to environmental stressors. They found that diets rich in omega-6 fatty acids, found in plant-derived oils, such as corn and safflower, can further promote the pro-oxidative and proinflammatory effects of certain polychlorinated biphenyl compounds (PCBs), prevalent environmental pollutants. In contrast, Hennig's group also found that diets rich in omega-3 fatty acids and antioxidant polyphenols, compounds found in many fruits, vegetables, and whole grains, can lessen toxicity of PCBs to the cell layer that line blood vessels.

"These beneficial compounds work in the body to help repair damaged cells and prevent certain disease mechanisms from occurring. Nutrition should be considered in overall risk assessment," said Hennig.

Hennig believes that nutritional interventions may provide the most sensible means to develop primary prevention strategies of diseases associated with many environmental toxic insults.

Envisioning future research

"This professorship will allow me to address future issues related to nutritional modulation of toxicological insults," said Hennig.

He envisions future research to include human intervention studies that try to mitigate Superfund pollutant-mediated toxicological risks and pathologies with positive lifestyle changes. For example, a nutrition-based therapeutic approach could reduce vulnerability to environmental stressors.

"In the United States, we like to take pills for everything, to treat diseases and improve health, but you cannot take a pill to mitigate exposure to environmental pollutants or to decrease body burdens of pollutants," said Hennig. "Why not stay healthier with good nutrition to fight environmental insults?"

Hennig has been a member of the University of Kentucky faculty since 1984. Since 2001, he has served as editor in chief of the Journal of Nutritional Biochemistry, a highly respected journal for research into the biochemical basis of nutrition. Since 2003, he has directed the SRC, funded by the National Institute of Environmental Health Sciences. His research has produced a steady series of publications in prominent journals and has earned him other national awards. Hennig also regularly participates in national and international conferences as an invited speaker.

(Carol Kelly is a health communication specialist with MDB Inc., a contractor for the NIEHS Division of Extramural Research and Training.)

"Since the hallmark of PCB-related vascular toxicity is also increased oxidative stress and inflammation, omega-3 polyunsaturated fatty acids and certain polyphenols are prime nutritional candidates to reduce toxicity to cells caused by PCBs," said Henning. (Photo courtesy of Bernhard Hennig)

Return to Table of Contents

EHS core center grantees gather in Seattle for annual meeting

By Sara Mishamandani

The University of Washington (UW) Center for Ecogenetics and Environmental Health (CEEH) hosted the 2013 NIEHS Environmental Health Sciences (EHS) Core Centers meeting April 17-19 in Seattle. The meeting brought together NIEHS staff and members from 20 core centers to share their latest work in environmental health, foster collaborations, and highlight novel research and community engagement activities.

The meeting featured scientific sessions on gene-environment interactions and global environmental health, breakout sessions with topics ranging from hydraulic fracturing to bidirectional communication, and a session highlighting research of young investigators. The meeting also included a community forum to learn about the Duwamish River cleanup project, which ended with an educational tour of Puget Sound, to inform participants about local Superfund sites and remediation efforts.

Collaborative EHS research

David Eaton, Ph.D., director of CEEH, chaired a session on the future of gene-environment interactions research. John Stamatoyannopoulos, M.D., associate professor of genome sciences and medicine at UW, described the Encyclopedia of DNA Elements, a forward-looking, data-rich project aimed at identifying all

functional elements encoded in the human genome. Stamatoyannopoulos explained the project's potential to yield many exciting insights on the role of gene-environment interactions in disease and epigenetics in human susceptibility to toxicants.

During another session, an inter-core center working group on hydraulic fracturing convened to discuss its research and community engagement recommendations. Trevor Penning, Ph.D., from the University of Pennsylvania (UP), facilitated the discussion on the current research gaps. Participants explained the need for baseline air and water quality data, and highlighted a collaborative study, between UP and Columbia University, to collect environmental data in Pennsylvania, where hydraulic fracturing is prevalent, and in New York, where hydraulic fracturing has not yet begun.

The group discussed the importance of compiling data from related studies and preserving its quality. Harvard University's EHS core center has initiated this process with FrackMap, a compilation of data related to hydraulic fracturing, through the Harvard University WorldMap project, an open-source web mapping system.

NIEHS and NTP Director Birnbaum and CEEH Director Eaton, welcomed meeting attendees at the opening reception. Birnbaum also spoke during the public forum on the Duwamish River cleanup. (Photo courtesy of Rachel McDuffie, University of Michigan)

University of Michigan COEC Coordinator Myra Tetteh, right, discusses community outreach activities with Les Reinlib, Ph.D., NIEHS EHS Core Centers program director, during the meeting poster session. Reinlib also introduced young investigators who gave talks on their scientific research during the meeting. (Photo courtesy of Rachel McDuffie, University of Michigan)

COEC efforts

Community outreach and engagement core (COEC) leaders shared past accomplishments and considered future efforts to sustain and strengthen their work. They started the meeting by convening a history wall to capture the many COEC milestone events and accomplishments since the beginning of the EHS Core Center program. The history wall served as a way to introduce many of the new COEC members to the program. Throughout the meeting, COEC leaders focused on evaluation; emerging topics, such as environmental health literacy, social media, and health impact assessments; and peer mentoring.

One of the sessions focused on preparing the next generation of environmental health scientists and building a diverse workforce. They all agreed that making science real community residents and youth, starting as young as elementary students, was central to this effort.

(Sara Mishamandani is a research and communication specialist for MDB Inc., a contractor for the NIEHS Superfund Research Program and Division of Extramural Research and Training.)

NIEHS community forum: Seattle waterways and your health

As part of the EHS Core Centers meeting, NIEHS and NTP Director Linda Birnbaum, Ph.D., joined local researchers, government officials, and industry experts at a public forum on the health impacts and pollution in Seattle's working river, the Duwamish. Seven short, lively presentations were followed by questions and discussion. The public forum was an opportunity to hear various perspectives about the historical, environmental, cleanup, and health issues on the Duwamish.

The Port of Seattle, Boeing, and other industries are located on the river. The Duwamish Superfund site, a 5.5 mile stretch of the river that flows into Elliott Bay, is one of the most polluted places in the United States. The U.S. Environmental Protection Agency (EPA) released its proposed cleanup plan for the site on February 28, and this timely forum occurred during the 90-day public comment period on EPA's proposed plan.

The diverse, historic Georgetown and South Park neighborhoods along the Duwamish are home to a disproportionate number of low-income, Hispanic, and recent immigrant residents. The river is also part of the traditional fishing grounds of three Northwest tribes.

Although a Washington State, Department of Health advisory warned residents not to eat fish or shellfish from the Duwamish River, health officials know that many people still subsidize their diets with the contaminated fish. They do so because of economic necessity, a misunderstanding of the danger, or an acceptance of the health risks.

Senior Medical Advisor Aubrey Miller, M.D., provided grantees with an update on NIEHS disaster research and training. (Photo courtesy of Sara Mishamandani)

To start off the meeting, COEC directors participated in a history wall activity. They brought in photos and materials from their COEC and added them to a timeline. Kathleen Vandiver, Ph.D., from MIT, left, and NIEHS COEC program lead Liam O'Fallon, add to the history wall. (Photo courtesy of Sara Mishamandani)

Ann Backus, Harvard University COEC director, had materials and events going back to the early 1960s, when the Harvard Center for Environmental Health was founded. (Photo courtesy of Naomi Hirsch, Oregon State University)

The public forum, held at a local cafe, covered topics related to remediation efforts on the Duwamish River, such as upstream pollution control, industry on the river, health effects research, and impacts on tribal communities. (Photo courtesy of Naomi Hirsch, Oregon State University)

The industrial sites on the Duwamish River were presented firsthand. Meeting participants saw pictures of local Superfund sites and learned about Superfund research from UW scientist Evan Gallagher, Ph.D., and his student, Chase Williams. James Rasmussen, Duwamish River Cleanup Coalition coordinator, also spoke to the group about the Duwamish Superfund site cleanup efforts. (Photo courtesy of John Schelp, NIEHS)

Return to Table of Contents

Yakel inspires future scientists

By Robin Mackar

It wasn't just a talk about cholinergic receptors in the brain that got the students at Saint Augustine's University (SAU) excited about careers in science. It was more a message of hope and pursuing dreams that caught their attention.

"I was where you are now, studying for my bachelor's degree in science, and feeling like I wasn't smart enough or good enough to be a scientist," said Jerrel Yakel, Ph.D., head of the Ion Channel Physiology Group and Acting Chief of the Laboratory of Neurobiology at NIEHS. "Fortunately, I had fabulous mentors that kept encouraging me to pursue my love of science. And I'm so glad I listened to them."

Yakel was invited to give the keynote address April 18 at SAU's 10th annual Undergraduate Research Day for the School of Sciences, Mathematics, and Engineering. Yakel spoke from experience, when he said students from underrepresented groups sometimes think graduate schools are too expensive and out of reach.

"Despite some of the contrary news you might be hearing, science is a great and rewarding career," Yakel said. "I feel honored every day that I get to come to work and study how the brain works." (Photo courtesy of the SAU School of Sciences, Mathematics, and Engineering)

"The truth is, graduate schools across the country are looking for people like you — young, smart, inquisitive students willing to work hard," he said.

During his visit to SAU's downtown Raleigh, N.C., campus, Yakel was able to catch up with the organizer of the event, Mark Melton, Ph.D., associate professor of biology and dean of the School of Sciences, Mathematics, and Engineering. Melton is among a dedicated group of educators who spent their summers working with NIEHS scientists on research projects. He worked with Yakel's group and the two have co-authored several articles together. Both share a passion for science and mentoring the next generation of scientists.

"No matter how busy Jerry is, he always makes time to share his science and his own career journey, so others can be inspired," Melton said. "It means a lot to the students."

Melton welcomed students to SAU's Undergraduate Research Day. (Photo courtesy of the SAU School of Sciences, Mathematics, and Engineering)

Exciting time for brain research

During his talk, Yakel also mentioned why it was an exciting time to be a scientist, especially studying the brain.

"Just a few weeks ago, the President and the director of the National Institutes of Health stood together and announced a $100 million initiative that is going to revolutionize our understanding of the brain," said Yakel. The new Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative aims to help researchers find new ways to treat, cure, and even prevent brain disorders, such as Alzheimer's disease, epilepsy, and traumatic brain injury.

Yakel received his B.S. from Oregon State University and his Ph.D. from the University of California, Los Angeles, where he studied ligand-gated ion channels and serotonin receptors. He is well known for his work on nicotine receptors in brain function, and his recent work in mice may have implications for learning and memory. His group demonstrated that, in the brain's hippocampus, the timing of the release of the neurotransmitter acetylcholine may play a role in regulating nerve cell connections or synapses (see story).

Yakel, as well as other scientists and postdoctoral students, work closely with the NIEHS Office of Science Education and Diversity, to reach out to talented students from underrepresented groups to get them interested in environmental health sciences. Their work has paid off as three SAU students — Kacey McHoney, Jennifer Plair, and Malcolm Richbourg — are currently doing research through the NIEHS Scholars Connect Program (see story).

(Robin Mackar is the news director in the NIEHS Office of Communications and Public Liaison, and a frequent contributor to the Environmental Factor.)

Return to Table of Contents

NIEHS marks social media milestone

By Eddy Ball

During the final week of March, NIEHS marked a social media milestone, as the number of its Facebook likes exceeded 1,000 for the first time.

"Liking a Facebook page signifies a much greater level of approval and trust in content reliability than merely visiting a page," said Joseph Poccia, who joined the NIEHS Office of Communications and Public Liaison (OCPL) in 2012 as a Web information development specialist.

According to OCPL Director Christine Flowers, for many people, especially those in the 18-34 age range, often the first things they check for news in the morning are Facebook and Twitter posts, which can appeal to people with special interests, such as environmental health.

"People are increasingly getting their news and information from the Internet on their computers, tablets, and cell phones," Flowers said. "Social media gives us a great way to communicate health and science information quickly and accurately. We're excited about reaching young people and sparking their interest in research and science careers."

Another upside to social media is the ability of its content to go viral through posting and reposting by direct and secondary followers.

OCPL launched its Twitter page in December 2010 and has accumulated more than 3,100 followers. The Institute's Facebook page, launched in December 2011, currently draws more than 4,000 visits per week.

According to Poccia, as of April 2, NIEHS Facebook had a total of 1,028 likes. "After the U.S. with 553, we have the most likes in Europe with 55, Central and South America with 35, India with 31, Pakistan with 28, and Egypt with 23," Poccia said. "In terms of demographics, 38.7 percent of our audience on Facebook is between the ages of 18-34, and 57.1 percent is female. Our Twitter feed has more than 5,800 followers."

One of the things that makes social media so appealing is its abbreviated format. In the case of Twitter, user posts, referred to as tweets, may not exceed 140 characters. That puts pressure on communicators to write content that is both enticing to the reader and concise. The tweet convention has even influenced the way OCPL puts together the landing page of its monthly newsletter, with story leads generally falling within the 140-character range.

Return to Table of Contents

Among his Web development and graphic arts duties, Poccia manages social media communication for OCPL. (Photo courtesy of Steve McCaw)

Since her arrival to NIEHS in 2004, Flowers has expanded OCPL's informational suite to include new media, such as social media and YouTube, in addition to conventional news services such as press releases, fact sheets, and a monthly newsletter. (Photo courtesy of Steve McCaw)

Clayton shines at area youth career fair

By Myra Westmoreland

As a research institute, NIEHS focuses on understanding how the environment affects people's health, but it adds to the cause by participating in programs that encourage young people to enter careers in environmental health sciences.

In one of those outreach events, Natasha Clayton, a biologist in the NIEHS Cellular and Molecular Pathology Branch, joined 11 other professionals at the Clarence E. Lightner YMCA Achievers Career Fair April 20 in Raleigh, N.C. Sponsored by the YMCA of the Triangle, the event exposed teenagers, from underrepresented groups, to a number of professions available to them once they finish high school.

In addition to hearing from Clayton, approximately 70 middle school and high school students were treated to talks from people in the fields of cosmetology, law, medicine, military service, music, psychology, and education.

Clayton showed students some of the items she uses in her work as a biologist at NIEHS. (Photo courtesy of Myra Westmoreland)

No science question was out of bounds, as Clayton responded to each query in language that her audience could understand. (Photo courtesy of Myra Westmoreland)

Being an example

As a representative of one of the myriad of careers in science, technology, engineering, and mathematics (STEM), Clayton discussed how to become a biologist and how to stay on top once there. She presented an overview of NIEHS, her day-to-day work in support of the mission, and information about several training opportunities available at the Institute. Clayton explained why she was compelled to participate in the career fair.

"I feel it is my responsibility to give back, by sharing my experiences with the youth in our communities," Clayton said. "I could see much promise in the teens with whom I interacted, and see many of them as future leaders."

Kendall Harris, YMCA of the Triangle community outreach director, thanked all of the participants for making the career fair a success, and conveyed sincere gratitude to the speakers who took time out of their busy schedules to attend.

"It is good to have people like you that care about our teens and their futures," Harris said.

Teens respond positively to science careers

Clayton inspired many teens interested in, or already pursuing, STEM opportunities. One said, "I like science, but never thought about doing research in a lab. It seems exciting." Another added, "Ms. Clayton seems so smart and on point. What she does seems important. I want to do something important."

Clayton left participants with sound advice. "Never be content with living inside the box your neighborhoods and surroundings may have attempted to build around you," Clayton urged. "Step outside without fear, and you will be surprised with the rewards you will gain from that."

(Myra Westmoreland is an administrative officer in the NIEHS Administrative Management Branch.)

Harris moderated the panel discussion, and said he was pleased with the variety of careers represented at the fair. (Photo courtesy of Myra Westmoreland)

Career fair mentees and mentors mingled during the three hour event. (Photo courtesy of Myra Westmoreland)

Return to Table of Contents

Science Notebook

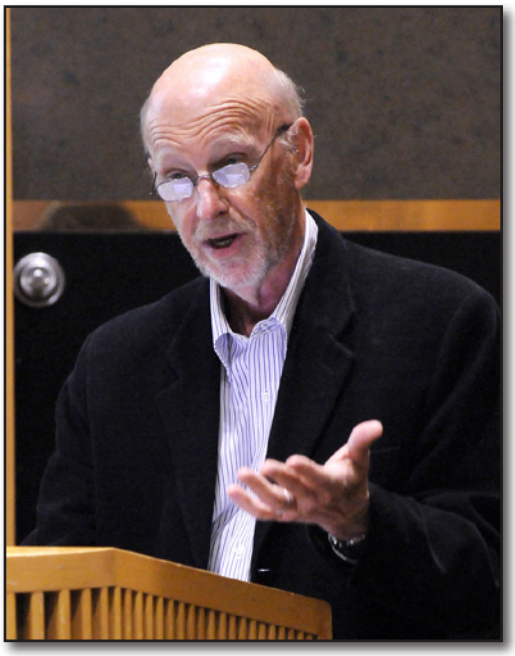
The role of calcium signaling in immune function

By Sheila Yong

Early in his career, Michael Cahalan, Ph.D., wanted to combine immunology and biophysics, two seemingly unrelated fields of science, to create a unique research niche that was his own. Since then, his vision has led to the ability to observe living immune cells in their host environment.

Cahalan discussed his work April 9 as part of the 2013 NIEHS Distinguished Lecture Series. "Cracking CRAC — the calcium release-activated calcium channel of the immune system," was hosted by James Putney, Ph.D., head of the Calcium Regulation Group in the NIEHS Laboratory of Signal Transduction.

Cahalan is a distinguished professor and chair of the Department of Physiology and Biophysics at the University of California, Irvine. In his introduction, Putney described Cahalan as an innovative researcher, whose quest has now turned into an enterprising venture that demonstrates the importance of the calcium signaling pathway in T cell function, and its potential as a therapeutic target for immune deficiency in humans.



Cahalan began his talk with an overview of the human immune system, before describing his research on calcium signaling in T cells. (Photo courtesy of Steve McCaw)

Observing immune cells in real time

"I would like to tell a story through some movies," Cahalan said as he began his talk. He introduced the audience to the revolutionary two-photon microscopy technique, which provides a much higher photon density compared to conventional microscopy methods, and subsequently enables imaging with greater sensitivity and depth penetration. Cahalan and colleagues took advantage of this technology to produce three-dimensional movies of live immune cells in various host environments, from isolated mouse lymph nodes to mice.

Cahalan's imaging experiments revealed how different types of immune cells move in the lymph nodes, their homing behavior, and their modes of action to eliminate foreign antigens.

NIEHS Laboratory of Signal Transduction Chief John Cidlowski, Ph.D., right, and Special Assistant to the Scientific Director Joel Abramowitz, Ph.D., enjoyed watching the video footage of immune cells in action. (Photo courtesy of Steve McCaw)

"The T cells move incredibly fast, so that they can scan the environment for antigens that are captured and brought to the lymph nodes by dendritic cells," Cahalan explained. "Once the two cell types meet, the dendritic cells interact with the T cells through long extensions, forming the immunological synapses."

He said these interactions, in turn, activate the T cells, causing them to divide rapidly and execute their effector functions.

Calcium Regulation Group visiting fellows Natacha Steinckwich-Besancon, Ph.D., left, and Felicity Davis, Ph.D., were intrigued by Cahalan's findings on the regulation of CRAC channels. (Photo courtesy of Steve McCaw)

Calcium signaling in T cell function

The discovery of various ion channels in T cells, many of which are calcium-regulated, sparked Cahalan's interest in the significance of calcium signaling in T cell function. His group found that calcium signaling is required to enhance T cell proliferation and the stability of the immunological synapses. The group also measured a small, but significant, inward calcium current which restores the calcium source inside the cells.

Through systematic and genome-wide RNAi screening, using cultured insect cells, Cahalan and colleagues discovered two proteins — the stromal interacting molecule (STIM) and Orai — which constitute what they termed the Ca2+ release-activated Ca2+ (CRAC) channel. Homologues of these proteins are present in humans, and the channel is highly selective for calcium ions. More importantly, the CRAC channels are responsible for engaging T cells and dendritic cells in the immunological synapses upon antigen recognition.

Cahalan and Putney listened attentively to questions from the audience. (Photo courtesy of Steve McCaw)

Cahalan emphasized that the CRAC channels are tightly regulated. Single amino acid mutations in their protein sequences may alter their flexibility and ion selectivity, leading to dire consequences.

"Many of these mutations have been implicated in patients with severe, combined immune deficiency," he added.

He also stressed that the stoichiometry, as well as the localization of STIM and Orai in the cells, is critical for the proper functioning of the channels, and has devoted substantial effort into dissecting how these aspects are regulated. Ultimately, Cahalan hopes to capitalize on his findings on CRAC channels, by developing therapeutic agents.

"This is a long and arduous process, but we are optimistic that these agents will make their way into clinical trials, and eventually benefit patients with immune deficiency disorders."

(Sheila Yong, Ph.D., is a visiting fellow in the NIEHS Laboratory of Signal Transduction.)

Return to Table of Contents

NTP webinar informs Report on Carcinogens

By Robin Mackar

The National Toxicology Program (NTP) successfully used a web-based meeting format April 11 to bring together scientific experts and members of the public for a discussion on pentachlorophenol (PCP) exposure and cancer.

PCP, which is primarily used as a wood preservative in the United States for items such as utility poles, cross arms, fence posts, and railroad ties, is a candidate substance being formally reviewed for possible listing in the Report on Carcinogens (RoC). The webinar created a virtual meeting, allowing more than 70 registered participants to watch, listen, and participate in discussions, by phone and computer, from across the globe.

The half-day session was moderated by epidemiologist Glinda Cooper, Ph.D., from the U.S. Environmental Protection Agency. The meeting included presentations from four outside scientists who have been involved in PCP human studies. The objective of the meeting was to receive scientific input on how best to evaluate the epidemiologic, or human, studies related to PCP exposure. NTP was specifically interested in hearing about PCP components and contaminants, and distinguishing between cancer effects caused by PCP and those that might be caused by other chemicals or contaminants to which workers may have been exposed.

Epidemiologist Cooper, formerly with NIEHS, moderated the RoC webinar on PCP. (Photo courtesy of Steve McCaw)

Purpose of webinar

"This webinar is intended to help inform our cancer evaluation of PCP," said Ruth Lunn, Dr.P.H., director of the NTP Office of the Report on Carcinogens, while providing an update on the RoC process. "It is not to receive recommendations from invited speakers or the public on whether or not PCP should be listed in the RoC." The cancer evaluation component, developed by Lunn and her staff, lays out all the information used to make a preliminary listing decision, and is an integral piece of the monograph that NTP prepares as part of its evaluation of a substance.

After some brief introductory comments, Cooper introduced the first panelist, and facilitated a question and answer session among participants after each presentation (see text box).

As discussion leader, Schubauer-Berigan helped clarify what is known about PCP exposure. (Photo courtesy of Mary Schubauer-Berigan)

Discussion and next steps

Mary Schubauer-Berigan, Ph.D., senior research epidemiologist at the National Institute for Occupational Safety and Health (NIOSH), competently served as discussion leader after the talks. She focused

on some very straightforward questions, ranging from what is known about how many people are currently exposed to PCP, to asking if all PCP exposure is contaminated or mixed with dioxins or other byproducts, or whether people can be exposed to pure PCP. These types of questions made for a lively discussion between the speakers, NTP staff, and the public.

"Getting scientific and public input using this kind of virtual meeting format is a new way of doing business for us," said Lunn after the meeting. "I was very pleased with how it all came together. We received a lot of good information that will provide a strong foundation as we move forward with our evaluation of PCP."

Following completion of the cancer evaluation component, NTP will prepare the draft substance profile. Both documents will be part of the draft RoC monograph released for public comment and peer review.

Presentation Highlights

Kevin Dunn, from NIOSH, presented an overview of occupational exposures to PCP. He said PCP was produced in the United States from 1936 to 2006, but since 1984, its use in the U.S. has been restricted to wood preservation and can no longer be used on wood in residential or agricultural buildings. Dunn discussed how exposure for PCP manufacturing workers might occur, including through dust or vapors, depending on the finishing process used to prepare the PCP and exposure in the wood preservative industry. He also identified common PCP contaminants.

Avima Ruder, Ph.D., also from NIOSH, focused on occupational exposure to PCP and other chemicals, while further addressing some of the issues that need to be carefully considered when evaluating human epidemiology studies. She discussed these issues as they relate to what NIOSH recently found in a mortality study that includes 2,122 U.S. PCP production workers, from four large chemical plants operating from 1936-2006. The workers were exposed to other chemicals, as well, while working at the plants.

James Collins, Ph.D., from the Dow Chemical Company, focused his talk on biomonitoring and epidemiologic studies of PCP producers. He talked about how difficult it is to determine exposure assessment for PCP. He shared biomonitoring data on serum dioxins from different types of PCP workers, and suggested that the dioxins, which are long-lived in the body, may serve as an indicator for past exposure to PCP. He discussed findings from an epidemiology study of PCP manufacturing workers at the Dow chemical plant.

The final presentation came from **Paul Demers, Ph.D., a professor at the University of Toronto Dalla Lana School of Public Health and the Cancer Care Ontario Occupational Cancer Research Centre**. Demers focused much of his remarks on a large study he has been involved with in British Columbia that includes 27,464 workers, employed by14 sawmills for 1 year or more, between 1950 and 1995. He also reviewed findings of other epidemiologic studies of PCP.

PCP webinar information is available on the NTP website.

(Robin Mackar is the news director in the NIEHS Office of Communications and Public Liaison, and a frequent contributor to the Environmental Factor.)

Return to Table of Contents

Symposium features cutting-edge stem cell research

By Ernie Hood

NIEHS and its neighboring research universities are hotbeds of scientific activity when it comes to the vast potential of stem cells, so it was only natural the Institute would hold a symposium on the topic. On April 11-12, NIEHS hosted Unlocking the Promise of Stem Cells, a meeting that brought together some of the nation's leading researchers in the field.

Raja Jothi, Ph.D., and Guang Hu, Ph.D., tenure-track investigators in the NIEHS Laboratory of Molecular Carcinogenesis (LMC), explore the biological mechanisms of stem cells and co-organized the gathering. They both believed having a discussion on how stem cells could be used to study environmental health science was needed, given the recent stem cell breakthroughs in regenerative medicine, drug discovery, and toxicity testing.

Hu leads the Stem Cell Biology Group at NIEHS. (Photo courtesy of Steve McCaw)

"We thought this would be a good opportunity to invite researchers, who are leaders in the field, to examine the current state of stem cell research and to think about how to move the discipline forward," Hu said. "The possibilities are endless, from scientific research tools to therapeutic applications."

The two days of presentations displayed a wide range of areas in which stem cells are poised to make major contributions (see text box). As NIEHS Scientific Director Darryl Zeldin, M.D., noted in his welcoming remarks, "Here at NIEHS, we're just beginning to appreciate how stem cells and their differentiated progenies can be used as new tools and as models for toxicologic studies, with the primary goal of understanding how environmental factors influence human health and disease."

Jothi heads the Systems Biology Group at NIEHS. (Photo courtesy of Steve McCaw)

Gathering of like minds

The symposium attracted more than 250 attendees on both days. Participants came from local government agencies, universities, and industries, as well as from universities in Virginia and the National Institutes of Health (NIH) in Bethesda, Md.

"The meeting provided a great opportunity for local stem cell researchers to interact and network, which we hope will lead to many collaborative efforts in the future," Jothi said.

The conference kicked off with a keynote address on the role of chromatin regulation in stem cells by Gerald Crabtree, M.D., a Howard Hughes Medical

With so much scientific interest in stem cells these days, the symposium was very well attended. (Photo courtesy of Steve McCaw)

Institute (HHMI) investigator and professor of pathology and developmental biology at Stanford University. The symposium was then divided into four sessions, each addressing a specific topic — adult stem cells, epigenetic regulation of stem cells, embryonic and pluripotent stem cells, and cellular differentiation and reprogramming.

NIEHS was well represented in the meeting. Both Jothi and Hu presented their work, as well as LMC head Trevor Archer, Ph.D., and George Fromm, Ph.D., a postdoctoral fellow in the Transcriptional Responses to the Environment Group headed by Karen Adelman, Ph.D.

Most of the conference's presentations dealt with highly specialized, basic research on the mechanisms underlying stem cell differentiation and self-renewal, but during the last session, speakers described new methods of using stem cells to model diseases, aid in drug discovery and screening, and advance regenerative medicine. As these approaches progress, researchers will indeed unlock the promise of stem cells, with exciting developments on the horizon.

(Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison.)

Keynote speaker Crabtree presented exciting new concepts and methods in chromatin regulation. (Photo courtesy of Steve McCaw)

Symposium attendees were also given the opportunity to review more than two dozen posters that were on display in the Building 101 lobby. Xiaofeng Zheng, Ph.D., right, a visiting fellow in Hu's group, discussed his research findings with an attendee. (Photo courtesy of Steve McCaw)

Archer's presentation focused on chromatin remodeling proteins and stem cell function in transcription. (Photo courtesy of Steve McCaw)

Describing work emerging from the Adelman group, Fromm noted, "There's been a lot of interest in pausing over the last few years, especially in the fields of developmental biology and stem cell biology." (Photo courtesy of Steve McCaw)

Spotlight on stem cells

Crabtree delivered the keynote lecture on the role of BAF chromatin remodeling complex in stem cells and during development. He also described a chromatin *in vivo* system for quantitative modeling of chromatin remodeling kinetics in living cells.

Iannis Aifantis, Ph.D., an HHMI investigator and professor of pathology at New York University, spoke about the role of the Notch signaling pathway in hematopoietic cell development and leukemia, and the potential therapeutic use of Notch receptor agonists in the treatment of myeloid leukemia.

Carla Kim, Ph.D., from Boston Children's Hospital and Harvard Medical School, discussed the identification and characterization of the bronchioalveolar stem cells in normal lung and lung cancer, as well as the development of an *in vitro* system for the culture and functional study of those cells.

Brigid Hogan, Ph.D., from Duke University, described the identification and characterization of airway basal stem cells that are essential for development, maintenance, repair, and disease of the lung.

Terry Magnuson, Ph.D., from the University of North Carolina at Chapel Hill, spoke about epigenetic regulation of male germ cell development, with an emphasis on the polycomb repressive complex 2, a protein complex involved in the long-term epigenetic silencing of chromatin.

Yi Zhang, Ph.D., an HHMI investigator at Boston Children's Hospital and Harvard Medical School, described the role of Tet1 in DNA demethylation, and showed that Tet1 controls meiosis by regulating meiotic gene expression.

Archer presented detailed structure-function analysis of the Brg1 protein in transcriptional regulation.

Minoru Ko, Ph.D., of Keio University in Japan, discussed his group's work on the unique role of Zscan4 in the maintenance of genome stability and developmental potential by regulation of telomere elongation.

Hu spoke about the identification of Fip1 as a novel regulator of embryonic stem cell (ESC) self-renewal and its role in the regulation of polyadenylation in ESCs.

Jothi presented his group's findings on the role of nucleolin in the regulation of cellular homeostasis in ESCs, and in maintaining the balance between self-renewal and differentiation.

Fromm discussed the role of RNA polymerase II pausing in ESCs and during development.

Konrad Hochedlinger, Ph.D., an HHMI investigator at Massachusetts General Hospital and Harvard University, presented a molecular roadmap of reprogramming somatic cells into induced pluripotent stem cells (iPSCs), with an emphasis on epigenetic changes.

Ignacio Sancho-Martinez, Ph.D., from the Salk Institute, described the lab's work on generation of cardiomyocytes from human ESCs for potential treatment of cardiac diseases and injuries.

Lorenz Studer, M.D., from the Sloan-Kettering Institute, spoke about the development of *in vitro* systems to derive neuronal cells from human ESCs or iPSCs for drug screening and potential cell therapies.

Mahendra Rao, M.D., Ph.D., from the National Institute of Arthritis and Musculoskeletal and Skin Diseases, part of NIH, described current development and available platforms for using ESCs or iPSCs for regenerative medicine and disease investigation at the NIH Center for Regenerative Medicine.

Return to Table of Contents

DNA methylation marker shows promise for detecting breast cancer risk

By Pamela Kidron

DNA methylation could prove to be an effective indicator of breast cancer risk, according to a new study published online April 11 in the Journal of the National Cancer Institute.

DNA methylation is a form of epigenetic modification that may control gene regulation, but is not directly part of the DNA sequence. In this study, NIEHS epidemiologists Jack Taylor, M.D., Ph.D., and Zongli Xu, Ph.D., discovered that, by measuring such epigenetic modifications, it's possible to capture changes in susceptibility to breast cancer that result from factors such as aging or the environment — changes that genetic studies of DNA sequence do not capture.

Taylor's group found that evidence of this modification was a better predictor of breast cancer risk than other approaches, such as the Gail model, which relies on known risk factors including age; reproductive, medical, and family history; and common polymorphisms. However, Taylor cautions that the work is the first study of its kind and that these measurements are not yet accurate enough for clinical use.

Taylor has duel appointments in the NIEHS Epidemiology Branch and the Laboratory of Molecular Carcinogenesis. (Photo courtesy of Steve McCaw)

NIEHS Sister Study yields valuable data

Working with DNA extracted from white blood cells in blood samples, Taylor and his colleagues assessed the methylation profile of 27,000 sites across the genome. They used samples from a cohort of women in the NIEHS Sister Study, a nationwide study of women who have had a biological sister with breast cancer. The Sister Study is designed to explore genetic and environmental determinants of breast cancer.

The NIEHS team used the data to examine whether these sites were different in those who later developed breast cancer than those who did not. They also examined the predictive power of blood methylation, compared with the Gail model, and 10 common polymorphisms that are associated with breast cancer risk.

The data provided evidence that there are differences in blood DNA methylation in those who ultimately develop breast cancer. These differences are detectable months to years before the clinical diagnosis of breast cancer.

Of the 250 differentially methylated sites the team identified, 188, or 75.2 percent, were undermethylated. The prediction accuracy via methylation was 66 percent, compared to 56 percent for the Gail model and 59 percent for genome-wide association study polymorphisms.

"While methylation profiling of blood holds promise for detecting and predicting breast cancer, we have to be careful," cautioned Taylor. "The next step is to replicate these methylation findings in other studies."

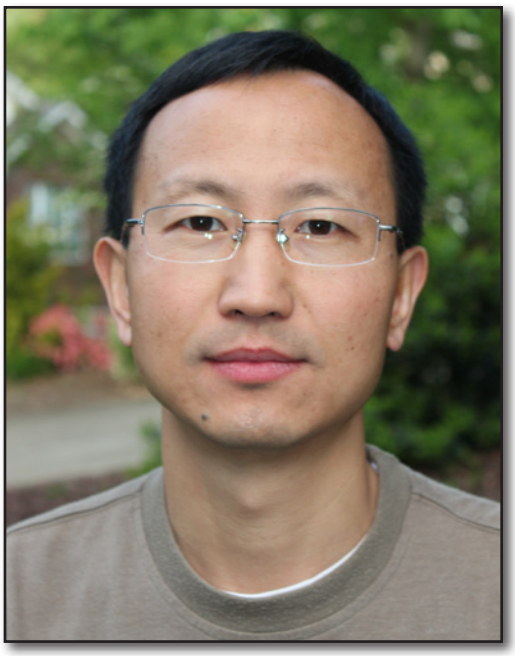
Because of the possibility that effects could differ by race or ethnicity, Taylor and the team restricted their analysis to non-Hispanic whites. Now, the findings must be replicated in studies of other ethnic groups. Also, the study was done with women who each had a sister with breast cancer, and it cannot be assumed that these results would apply to women with a different family history.

Producing a diagnostic tool

The study may help researchers move closer to developing a blood test that can predict a woman's chances of developing breast cancer. Women with elevated risk could then be monitored closely. Early diagnosis of breast cancer, before it spreads, is essential for successful treatment.

Breast cancer is the most common cancer in women and the leading cause of cancer mortality worldwide. Some 40,000 people die annually from breast cancer in the United States.

Taylor heads the NIEHS Molecular and Genetic Epidemiology Group, which works toward understanding the interaction between genes and environmental exposures in human carcinogenesis. The Sister Study is led by NIEHS Epidemiology Branch Chief Dale Sandler, Ph.D.



Xu is a staff scientist in the NIEHS Epidemiology Branch and first author on the paper. (Photo courtesy of Zongli Xu)

Citation: Xu Z, Bolick SC, DeRoo LA, Weinberg CR, Sandler DP, Taylor JA. 2013. Epigenome-wide association study of breast cancer using prospectively collected Sister Study samples. J Natl Cancer Inst; doi:10.1093/jnci/djt045 [Online 11 April 2013].

(Pamela Kidron is a contract writer with the NIEHS office in Bethesda, Md.)

Return to Table of Contents

NIEHS fellow begins career in clinical research

By Aleksandra Adomas

Darshini Trivedi, Ph.D., left the NIEHS Laboratory of Toxicology and Pharmacology in April to start her new career as a clinical research scientist at Impact Pharmaceutical Services Inc. (IMPACT). The company is a local contract research organization that specializes in providing regulatory and drug development consulting, medical writing, and project and program management to the pharmaceutical and biotech industries.

Perfect timing

Trivedi's job search is a story of networking, hard work, and perfect timing. She was one of the first members of the Rho Tau Chapter of Graduate Women in Science in Research Triangle Park, N.C., and when one of the chapter officers transitioned to IMPACT, she notified Trivedi about a job opening. That connection led to an interview in February 2012, but Trivedi was not ready to start a new job at that time. She was working on a project that needed a few more months of additional experiments, and she suggested late summer as a potential start date.

"I was not surprised that IMPACT didn't offer me a job back then," Trivedi admitted.

After her manuscript was submitted, Trivedi could again focus on her career, this time with the approaching retirement of her mentor, Robert Langenbach, Ph.D., as a deadline. During a short internship at the Duke

Translational Medicine Institute, Trivedi discovered that, with her science and pharmacology background, regulatory affairs could be a perfect fit.

So, she sent her updated resume to the IMPACT hiring manager, with whom she kept in touch as part of her networking efforts. A month later, the same week her revised manuscript was resubmitted to the journal, Trivedi received an invitation for another interview. The acceptance notice for the paper came at the same time as the official job offer, a month before the end of her postdoctoral training.

"It couldn't have been more perfect," Trivedi explained. "I was able to complete my work, publish a paper in a good journal, do an internship, and get a job I'm really excited about."

As part of her networking strategy, Trivedi used LinkedIn to connect with professionals working at different companies. "There were a couple of months that I met one or two people every week," she said. "Almost every single person responded to my invitation and almost everyone was very useful." (Photo courtesy of Steve McCaw)

NIEHS career resources

Trivedi praised opportunities and career counseling, available to trainees at NIEHS, as helping in her success. She was especially thankful for the writing experience she gained over two years of contributing to the NIEHS Environmental Factor. Having decided on regulatory affairs as a career path, Trivedi concentrated on preparing summaries of scientific papers outside her area of expertise, to show her future employer she had good communication skills and competence in a broad range of science.

She also sought out opportunities to gain other skills valued in the industry — leadership and teamwork. As an active member of the NIEHS Trainees Assembly Steering Committee, Trivedi co-chaired the 2012 NIEHS Biomedical Career Fair, and participated in the Citizen Schools (see story) project, for which she and other volunteers received an award (see story).

Collins and OFCD provide NIEHS trainees with career development training and counseling opportunities. One of the sessions Trivedi took advantage of was a mock job interview. (Photo courtesy of Steve McCaw)

Many of the workshops that Tammy Collins, Ph.D., director of NIEHS Office of Fellows' Career Development (OFCD) and Lori Conlan, Ph.D., director of the NIH Office of Postdoctoral Services, brought to NIEHS helped Trivedi answer behavioral questions she was asked during the job interview.

Trivedi also recognized the quality of the mentorship she received while at NIEHS. During those four years, Trivedi and Langenbach identified the signaling protein beta-arrestin-2 as a major player that could be used as a drug target for new treatments in aneurysm development (see text box).

"I've had excellent mentors who always offered me great support and advice," Trivedi said. "I was fortunate to work with Bob [Langenbach], who gave me independence in the lab, and based on other ongoing beta-arrestin studies, the freedom to develop a new aneurysm disease model."

Understanding how aneurysms form

Trivedi and Langenbach studied abdominal aortic aneurysm (AAA), a potentially life-threatening disease that affects blood vessels. Since no current pharmacological treatment exists for the condition, Trivedi and Langenbach set out to understand AAA formation.

Other researchers utilized a mouse model to study AAA formation and established that angiotensin II (AngII), a drug that raises blood pressure by constricting blood vessels, binds to a G-protein coupled receptor called AT1a. Additional studies found that the multifunctional scaffolding protein, beta-arrestin-2, also binds to AT1a, so Trivedi and Langenbach wanted to know if beta-arrestin-2 was involved in AAA formation.

They determined that beta-arrestin-2 contributes to AngII-induced AAA formation, by activating extracellular-signal-regulated kinases (ERKs), cyclooxygenase-2 (COX-2), and other factors involved in the inflammatory response. Their results suggest that beta-arrestin-2 may be a novel target for pharmacotherapeutic design in AAA treatment.

Citation: Trivedi DB, Loftin CD, Clark J, Myers P, Degraff LM, Cheng J, Zeldin DC, Langenbach R. 2013. Beta-arrestin-2 deficiency attenuates abdominal aortic aneurysm formation in mice. Circ Res; doi:10.1161/CIRCRESAHA.112.280399 [Online 22 March 2013].

(Aleksandra Adomas, Ph.D., is a research fellow in the NIEHS Laboratory of Molecular Carcinogenesis.)

Return to Table of Contents

Casey presents at workshop on stems cells in cardiotoxicity studies

By Cathy Sprankle

Pollutants and toxicants in the environment have the potential to damage cells in the heart. Known as cardiotoxicity, it is also a major reason for drug development failure. Because of its importance, scientists from all over the world gathered in Boston March 18-19 to share the best and latest research methods in the field.

One of those scientists was Warren Casey, Ph.D., acting director of the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM). Casey joined an international group of presenters, representing research institutions, pharmaceutical companies, and government agencies, at the Stem Cell-Derived Cardiomyocytes as Models of Cardiac Pathobiology and Toxicology Workshop.

The Health and Environmental Sciences Institute (HESI), a nonprofit institution that brings scientists together to address global health and environmental issues, sponsored the workshop as a way to assess the current status and potential applications of the use of stem cell-derived cardiomyocytes, or cultured heart cells, for studying cardiotoxicity.

Casey's presentation described how testing approaches, that use cultured cells, might be used in regulatory or safety decision-making contexts.

"Stem cells and other technologies can help us better understand the mechanisms underlying toxicity and disease," he said. "For example, they can help us understand how the genetic diversity of target populations affects toxicity. But, as we move toward using emerging technologies, such as stem cell-derived cardiomyocytes for safety testing, it's important that we develop appropriate validation criteria, so that the data these test methods provide are useful to regulators."

The workshop's goal was to evaluate how such technologies may be used to evaluate risks to human cardiac health from pharmaceuticals and environmental chemicals. Topics discussed included the biology of cultured cardiomyocytes, specific approaches to using them to assess toxicity, how those approaches might be used to benefit public health, and future research and development needed to achieve those public health benefits.

A report from the workshop will be published in a scientific journal, and the recommendations will help pharmaceutical companies and other stakeholders develop improved approaches for this important safety testing area.

(Cathy Sprankle is a communications specialist with ILS Inc., support contractor for NICEATM.)

Casey, acting director of NICEATM, spoke at a recent workshop on how cultured heart cells could be used to understand how chemicals may affect heart muscle function. (Photo courtesy of Steve McCaw)

Return to Table of Contents

Farmland application of sewage sludge raises environmental justice concerns

By Nancy Lamontagne

People who live close to farmland where treated sewage sludge is applied to the soil said they experience physical symptoms, smell offensive odors, and are angry about the practice, according to a new study from NIEHS grantees at the University of North Carolina at Chapel Hill (UNC) Gillings School of Global Public Health. The study, which was supported by the NIEHS Partnerships for Environmental Public Health, indicates a need for involving community members in the decision-making process about land application of sewage sludge.

Researchers found that health concerns recorded in this study were consistent with other reports, but they did not expect so many respondents to express feelings of injustice over the spreading of urban wastes called "sludge" in rural areas.

Treated sewage sludge, the solid byproduct of wastewater treatment, is often applied to farmland as a soil amendment in the United States. (Photo courtesy of Sustainable Sanitation Alliance)

"Many of the people interviewed reported a lack of public notification about land application in their neighborhood, and said they had difficulty reporting concerns to public officials and influencing decisions about how the practice is conducted where they live," said Amy Lowman, research associate in epidemiology at UNC and the study's first author.

More than half of the people interviewed in Lowman's study reported physical symptoms, which they associated with the land application of sludge. (Photo courtesy of UNC)

Responding to a community need

"Rural residents who knew about our previous studies of health impacts of hog waste contacted us about illness and noxious odors that they associated with the use of treated sewage sludge on farmland near their homes," said Steve Wing, Ph.D., associate professor at UNC and a co-author of the study. In response, the researchers interviewed 34 people from North Carolina, South Carolina, and Virginia who lived near fields where sludge is applied as a soil amendment.

More than half of the study participants reported physical symptoms such as eye, nose, and throat irritations and gastrointestinal symptoms. Most of them said that the unpleasant odors from the sludge disrupted their daily activities and socializing with family and friends.

"Researchers and public officials responsible for permitting land application of sludge from municipal wastewater should not be so dismissive of neighbors' reports of illness," Wing said.

Wing said that researchers and public officials responsible for permitting land application of sludge from municipal wastewater should not be dismissive of neighbors' reports of illness. (Photo courtesy of UNC)

In addition to being angry over not being informed that sludge was being applied near their homes, the people interviewed also said that regulators seemed unconcerned with violations of land application rules, and that public officials do not respond to reported concerns. Study participants wanted improved monitoring and better enforcement of regulations, and several said they would like public officials to directly notify residents near application sites prior to every application, so they can prepare and take precautions.

"It may also be helpful to provide a way for neighbors of treated sludge fields to report possible violations, such as application during rain events or runoff of sludge into waterways, so potential problems can be promptly addressed," Lowman said.

Wing outlined several changes that could lessen the impact of land application of sludge. In the short term, these modifications include decreasing the frequency and amounts of sludge applied, increasing buffers between application sites and neighbors, and improving the treatment of sludge to reduce pathogens and bacterial regrowth.

"In the long run, it will be important to eliminate industrial wastes that are released to domestic treatment plants, and to address the sustainability of using potable water, which will be increasingly scarce as climate change occurs, to flush human waste," Wing said.

Citation: Lowman A, McDonald MA, Wing S, Muhammad N. 2013. Land application of treated sewage sludge: community health and environmental justice. Environ Health Perspect; doi:10.1289/ehp.1205470 [Online 11 March 2013].

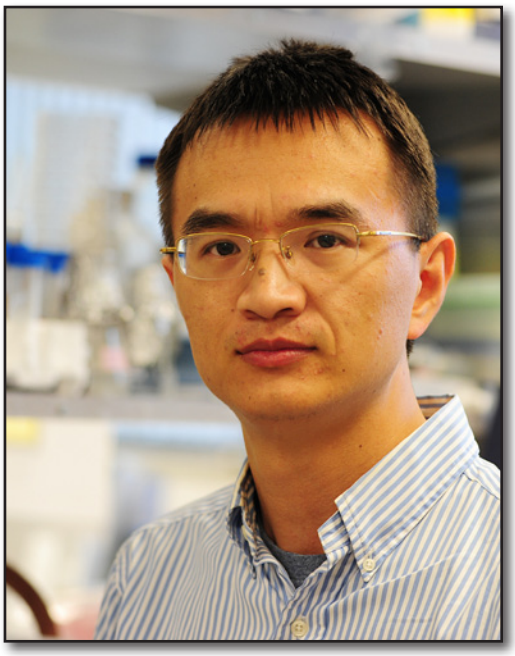
(Nancy Lamontagne is a science writer with MDB Inc., a contractor for the NIEHS Division of Extramural Research and Training, Superfund Research Program, and Worker Education and Training Program.)

Return to Table of Contents

Fatty acid metabolite inhibits tumor growth in mice

By Sara Mishamandani

According to a recent NIEHS-funded study, a product from the metabolism of omega-3 fatty acid helps combat cancer, by cutting off the oxygen supply and nutrients that fuel tumor growth. With this finding, a team of University of California, Davis (UC Davis) scientists provides more evidence about how omega-3 fatty acids, which are commonly found in certain fish and plant oils, may be used to fight cancer.



Zhang studies how blood vessels form during tumor growth and metastasis. (Photo courtesy of Guodong Zhang)

"Our investigation opens up a new understanding of the pathways by which omega-3 fatty acids exert their biologic effect," said Guodong Zhang, Ph.D., lead author of the study. Zhang is a postdoctoral researcher in the laboratory of Bruce Hammock, Ph.D., NIEHS Superfund Research Program center director at UC Davis.

Fatty acids and tumor growth

Zhang explained that tumors grow and spread by disrupting the normal process of angiogenesis, the formation of new blood vessels in the body. He and his colleagues determined that the metabolite epoxydocosapentaenoic acid (EDP) inhibits angiogenesis, which reduces the growth and spread of tumors in mice. It also blocks angiogenesis by a different mechanism than many current anti-cancer drugs.

EDP is produced in the human body from the omega-3 fatty acid docosahexaenoic acid (DHA), which is found in cold-water oceanic fish oils and various supplements and pharmaceuticals. EDP is also increasingly made industrially.

"As far as we know, EDPs are the first signaling lipids that have been discovered to have such potent anti-cancer effects," said Zhang. "Researchers may be able to use EDPs as structural targets to develop stable analogs as anti-cancer agents."

Researchers also found that a metabolite of arachidonic acid (ARA), an omega-6 fatty acid, has the opposite effect of EDP. The ARA metabolite slightly increases angiogenesis and tumor progression in mice. ARA in the human body usually comes from dietary animal sources, such as meat, eggs, and dairy. This increase in angiogenesis encourages wound healing and tissue repair.

Cancer treatment and nutrition

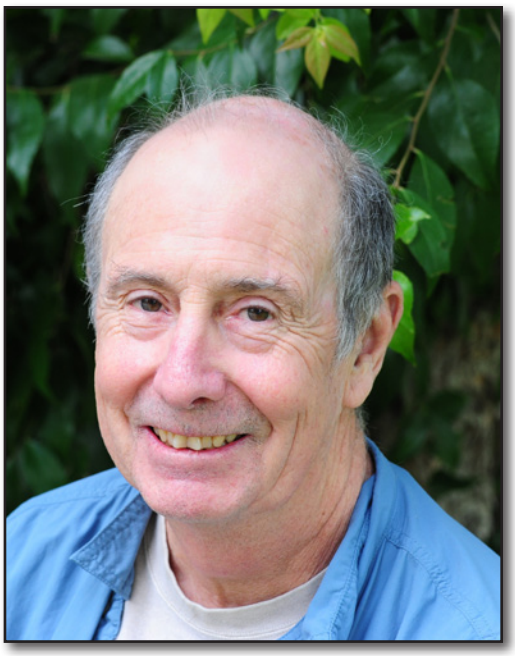
Based on the study findings, inhibiting the enzyme soluble epoxide hydrolase (sEH) stabilizes and increases levels of DHA-derived EDPs. Researchers found that coadministering a low-dose sEH inhibitor with EDPs stabilized EDP in circulating blood, leading to dramatic inhibition of tumor growth and metastasis. Current anti-cancer drugs sorafenib and regorafenib are FDA-approved kinase inhibitors, which also inhibit sEH.

"It may be possible to improve the efficacy of these anti-cancer drugs by combining them with a diet high in omega-3 and low in omega-6 fatty acids," Hammock said.

Citation: Zhang G, Panigrahy D, Mahakian LM, Yang J, Liu JY, Stephen Lee KS, Wettersten HI, Ulu A, Hu X, Tam S, Hwang SH, Ingham ES, Kieran MW, Weiss RH, Ferrara KW, Hammock DB. 2013. Epoxy metabolites of docosahexaenoic acid (DHA) inhibit angiogenesis, tumor growth, and metastasis. Proc Natl Acad Sci USA; doi:10.1073/pnas.1304321110 [Online 3 April 2013].

(Sara Mishamandani is a research and communication specialist for MDB Inc., a contractor for the NIEHS Superfund Research Program and Division of Extramural Research and Training.)

Return to Table of Contents



Hammock is also a distinguished professor in the Department of Entomology at UC Davis. (Photo courtesy of Bruce Hammock)

Brown bag lunch highlights careers in intellectual property and patent law

By Aleksandra Adomas

The last brown bag lunch in the 2012-2013 series (see text box) explored career options available to scientists in intellectual property and patent law. Laura L. Kiefer, Ph.D., J.D., of Olive Law Group, and Rob Schwartzman, Ph.D., J.D., of Myers Bigel Sibley & Sajovec, two patent attorneys with research experience in the life sciences, spoke with NIEHS trainees April 11 about the responsibilities of a patent expert.

From researcher to patent lawyer

Mallikarjuna Metukuri, Ph.D., a research fellow in the NIEHS Laboratory of Signal Transduction, hosted the event. He and his fellow trainees were fascinated to hear that both guests obtained their J.D. degrees after earning their Ph.D.s and completing postdoctoral training.

For Metukuri, one of the more valuable pieces of information he learned was that the patent bar exam, which can make entering patent law easier, is an open book test that may be taken anytime. (Photo courtesy of Steve McCaw)

After graduating from Duke University, Kiefer went to work as a biochemist for a startup pharmaceutical company. Being the only person working on a project led her to consider other careers, so she took a job as a patent agent for a while, before deciding to go to law school full time.

Dedicating 11 years to his research training, both at the University of North Carolina at Chapel Hill and as a postdoctoral fellow at the Carnegie Institution of Washington, Schwartzman found that focusing on a single aspect of a biological question limiting and unsatisfying. So, he changed careers to become a patent and trademark office examiner. Afterward, he entered law school and attended part time.

Kiefer said, young scientists interested in intellectual property law have had a harder time finding a job in Research Triangle Park, N.C. She recommended gaining additional law experience, such as through an internship, while still doing graduate or postdoctoral research. (Photo courtesy of Steve McCaw)

Patent law career options

Kiefer and Schwartzman explained that a scientist could be hired by a law firm as a technical specialist, patent agent, or patent attorney. A technical specialist has no law experience and is required to understand the science behind an invention.

"After all, it's easier to teach a scientist some law than a lawyer some science," Schwartzman pointed out.

While both a patent agent and an attorney need to pass a patent bar exam, only an attorney has a law degree. Although an agent is not able to sign off on all legal documents, both agents and attorneys prepare patent applications and communicate with the U.S. patent office. Many, but not all, law firms treat their agents and attorneys the same, and expect the same amount of work from them. Attorneys can anticipate their salaries to be higher, making the investment of going to law school worthwhile.

The fourth option of practicing patent law is to work as a patent examiner for the United States Patent and Trademark Office. Examiners, who must be U.S. citizens, review patent applications for compliance with basic rules and legal requirements. Referring to his own time at the office, Schwartzman called it a very valuable experience that makes finding the next job easy. He explained that law firms are looking for former examiners familiar with the patent application process, and reviewers with four years of experience are exempt from the bar exam requirement.

Schwartzman did his postdoctoral research at the Carnegie Institution of Washington with John Cidlowski, Ph.D., current chief of the NIEHS Laboratory of Signal Transduction. Schwartzman said visiting NIEHS to talk about his career was like completing a full circle. (Photo courtesy of Steve McCaw)

Qualities of a good patent specialist

Kiefer emphasized that writing well and communicating clearly is crucial for anyone entering patent law. Additionally, patent agents and attorneys frequently have to argue why their clients' inventions should be patented. It takes focus, discipline, and intelligent reasoning.

"You need to be able to pick up a new technology, understand it, and have a conversation about it," Kiefer said.

Kiefer and Schwartzman described the job as hard and extremely deadline driven. The workload is expressed in billable hours that can amount to 1,800-2,100 a year. To bill an eight hour workday, an agent or attorney may need to put in 10-11 hours, which may include nonbillable meetings and lunch breaks. But, exceeding expectations could be a road to partnership in a law firm.

Both Kiefer and Schwartzman spoke highly of job satisfaction, such as the joys of having a patent application approved, talking to highly engaged inventors, or working for a startup company that is purchased by a bigger corporation for its profitable patents.

(Aleksandra Adomas, Ph.D., is a research fellow in the NIEHS Laboratory of Molecular Carcinogenesis.)

NIEHS trainees learned that a lawyer employed as an in-house counselor by a pharmaceutical company, rather than a law firm, may have a more diverse set of responsibilities, including reviewing licenses, and employee and contract agreements. (Photo courtesy of Steve McCaw)

Christopher Campos, Ph.D., an Intramural Research Training Award fellow in the Laboratory of Toxicology and Pharmacology, added to the conversation, by saying the fields of computer and electrical engineering always need new patent lawyers. (Photo courtesy of Steve McCaw)

Brown bag lunch series

The NIEHS Trainees Assembly Steering Committee initiated the lunch series in 2011, as a way of highlighting career options in different areas of science (see story). Tammy Collins, Ph.D., the current director of the Office of Fellows' Career Development, was, at the time, an Intramural Research Training Award fellow in the Laboratory of Molecular Genetics and in charge of selecting themes, inviting guests, and moderating meetings. Sonika Patial, Ph.D., a visiting fellow in the NIEHS Laboratory of Signal Transduction, took over in 2012 and chaired the series that featured a number of engaging topics.

Month	Topic	Host
Sept. 2012	Industry — Bench	Priya Ramamoorthy
Oct. 2012	Academia — Teaching and Research	Melissa Hausburg
Nov. 2012	Industry — Nonbench	Sheetal Thakur
Dec. 2012	Grantsmanship	Jennifer Sims
Jan. 2013	Nonprofits	Ashley Godfrey
Feb. 2013	Scientific writing and editing	Sonika Patial
March 2013	Consulting and project management	Georgette Charles
April 2013	Patent law	Mallikarjuna Metakuri

Return to Table of Contents

New protein mutated in neurodegenerative disease

By Robin Arnette

When injury to the mammalian genome occurs, such as when DNA strands break, specialized proteins called poly(ADP-ribose) polymerases, or PARPs, raise an alarm. Upon encountering DNA damage, PARP1 tags a host of DNA damage repair first responder proteins, as a means of controlling their activity. These molecular tags are formed by generating repeating chains of the small molecule ADP-ribose, to create poly(ADP-ribose) or PAR tags.

Proper coordination of responses to DNA damage also requires complete removal and recycling of such tags. For several decades, though, scientists did not know which protein clips the ADP-ribose directly attached to tagged proteins. Now, a team that includes several NIEHS researchers has identified and characterized one such protein, and uncovered another surprising detail — a mutation in its gene leads to a rare form of neurodegenerative disease.

Williams and his collaborators have identified a protein they call TARG1, a new factor in the DNA damage response that's mutated in neurodegenerative disease. (Photo courtesy of Steve McCaw)

Working together to find a solution

The research, which appeared online March 12 in The EMBO [European Molecular Biology Organization] Journal, was a multidisciplinary effort from scientists and clinicians from the United Kingdom, United States, Germany, and Iran. Scott Williams, Ph.D., of the NIEHS Laboratory of Structural Biology, led the NIEHS contingent that characterized the activity and structure of the protein, originally known as C6orf130.

Williams said, he and his group were interested in C6orf130, because it is a member of a poorly understood family of proteins that contain ADP-ribose interacting macrodomains. In collaboration with Ivan Ahel, Ph.D., of the Paterson Institute for Cancer Research at the University of Manchester, and Reza Sharifi, M.D., Ph.D., of St. George's University of London, European team members identified a mutation in the *C6orf130* gene.

When the mutated gene was expressed, the resulting C6orf130 protein was chopped in half, rendering it inactive. As a result, people born with two copies of the mutated gene were bound to wheel chairs. They suffered seizures, and displayed a lack of a tendon reflex and a partial absence of a swallowing reflex.

"We renamed C6orf130, terminal ADP-ribose protein glycohydrolase 1, or TARG1, because it cleaves at the stem of where the ADP-ribose modification is made on a protein," Williams said. "The neurodegenerative condition that occurs is a TARG1 deficiency."

So far, the only people who have the unnamed illness come from members of one family in Iran, but Williams said other mutations in TARG1 may produce other infirmities, so more research is needed.

Seeing TARG1 in action

Using X-ray crystallography, as well as a variety of biochemical techniques, Williams' research group, which included Denise Appel, Juno Krahn, Ph.D., and Matthew Schellenberg, Ph.D., generated high-resolution molecular snapshots showing how TARG1 engaged and processed the terminal ADP-ribose. With additional

mass spectrometry analysis from Jason Williams, Ph.D., and his group at the NIEHS Protein Microcharacterization Core Facility, the team discovered that TARG1 formed a transient intermediate with its substrate. This transitional molecule was critical in TARG1's removal of ADP-ribose.

Appel is a biologist in the Williams group and shared first authorship on the journal article. She said, defining the molecular mechanism of TARG1 and understanding how one mutation in its gene led to disease was significant, but these studies may also have the potential to help cancer patients.

"Researchers can selectively kill tumor cells by affecting their ability to metabolize poly(ADP-ribose) correctly," Appel said. "Since TARG1 acts to degrade poly(ADP-ribose), it may be an attractive target for drug development in cancer chemotherapy."

Williams was just as excited about the TARG1 research, and said one rarely sees a story laid out in one publication — identification of a critical enzymatic activity and the protein involved, atomic resolution snapshots of its mode of action, and the documentation of the individuals within the human population with defects in that activity.

Appel helped to determine TARG1's mechanism of action. (Photo courtesy of Steve McCaw)

"It's a fine example of science's move toward powerful multidisciplinary research," Williams said. "It's one of the most comprehensive projects I've ever been involved in."

Citation: Sharifi R, Morra R, Appel CD, Tallis M, Chioza B, Jankevicius G, Simpson MA, Matic I, Ozkan E, Golia B, Schellenberg MJ, Weston R, Williams JG, Rossi MN, Galehdari H, Krahn J, Wan A, Trembath RC, Crosby AH, Ahel D, Hay R, Ladurner AG, Timinszky G, Williams RS, Ahel I. 2013. Deficiency of terminal ADP-ribose protein glycohydrolase TARG1/C6orf130 in neurodegenerative disease. EMBO J; doi:10.1038/emboj.2013.51 [Online 12 March 2013].

Return to Table of Contents

NIEHS fellow transitions to career in biopharmaceuticals

By Monica Frazier

As a postdoc and then a research fellow at NIEHS, Rajesh Kasiviswanathan, Ph.D., was a busy and productive member of the Mitochondrial DNA Replication Group, headed by Chief of the Laboratory of Molecular Genetics (LMG) William Copeland, Ph.D. Now, after a successful job search, Kasiviswanathan will bring the same work ethic and intensity to his new position.

In March, Kasiviswanathan joined the Purification Development Division at Fujifilm Diosynth Biotechnologies in Morrisville, N.C., a contract manufacturing organization that produces recombinant proteins, vaccines, and monoclonal antibodies using good manufacturing practices. His new career dovetails perfectly with his experience at NIEHS. While at the Institute, he specialized in protein purification and characterization, so much so that he published several papers, including seven as first author.

"Rajesh's vast experience in protein chemistry and enzymology will serve him well at Fujifilm," Copeland said. "I expect great success from him."

Kasiviswanathan said, "I am very fortunate to find a position at Fujifilm Diosynth that perfectly matched my technical expertise and career interests." (Photo courtesy of Steve McCaw)

Knowing your strengths

After earning his graduate degree at the University of Maryland, College Park, Kasiviswanathan wasn't entirely sure whether he wanted to do his postdoc in government, industry, or academia, but he knew coming to NIEHS would definitely give him confidence, independence, and critical skills, such as experimental design, protein purification, and interpreting and communicating scientific data.

In Copeland's group, Kasiviswanathan studied the biochemical defects of disease mutations in the human mitochondrial DNA polymerase gamma, but he was also involved in collaborative studies with colleagues at Yale, Duke, and Oregon Health and Science University, among others.

Kasiviswanathan noted, "I realized very early during my postdoc that I like purifying proteins, and I had lots of opportunities to learn and standardize the processes for protein purification in Bill's lab."

Using your network

Kasiviswanathan took advantage of opportunities to gain leadership experience and build a network through NIEHS. He was involved in organizing two LMG retreats, and used his leadership position to develop contacts that were very helpful during his job search. "I highly recommend that postdocs serve on these committees, because it is a great way to develop new contacts and network," he said.

Kasiviswanathan suggested postdocs use tools offered through the NIEHS Office of Fellows' Career Development, and felt that identifying his career goals early during his postdoc was a huge advantage. The combination of his impressive scientific accomplishments and ability to network ultimately helped Kasiviswanathan find the exact position he wanted.

(Monica Frazier, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Laboratory of Molecular Genetics.)

"Rajesh was an absolute gem in the lab and will be deeply missed," Copeland said. (Photo courtesy of Steve McCaw)

Return to Table of Contents

This month in EHP

This month's features in Environmental Health Perspectives (EHP) examine the health impacts of Hurricane Sandy and environmental exposures in child care centers.

http://twitter.com/ehponline

The Long Road to Recovery: Environmental Health Impacts of Hurricane Sandy

Hurricane Sandy, which struck the East Coast of the United States Oct. 29, 2012, was the largest storm ever recorded in the Atlantic Ocean. It reached more than 1,000 miles in diameter and affected 24 states from Florida to Maine. Every layer of society felt the effects of the hurricane, and as the recovery and rebuilding move forward, the environmental health impacts of Hurricane Sandy continue to unfold.

Environmental Exposures in the Context of Child Care

Because infants and toddlers experience the world with their hands and mouths, they are more exposed and more sensitive to toxic substances indoors. Yet, environmental health standards in child care settings nationwide, which include not just private centers, but also a variety of other venues, lag behind those of schools. While national child care regulations appear unlikely anytime soon, experts say the child care industry is on the verge of a breakthrough in environmental health.

Featured research and related news articles this month include:

- **Source Attribution of Health Benefits From Air Pollution Abatement in Canada and the United States: An Adjoint Sensitivity Analysis** — Reverse Influence Modeling: Estimating Source-by-Source Health Benefits of Reduced Emissions

- **Individual Day-Time Noise Exposure During Routine Activities and Heart Rate Variability in Adults: A Repeated Measures Study** — Pathways for Processing Noise: Heart Health and the Sounds of Everyday Life

- **Urinary Metabolites of Organophosphate Flame Retardants: Temporal Variability and Correlations with House Dust Concentrations** — New Details on Organophosphate Flame Retardants: Exposure in Men Appears Stable Over Time

- **Pit Latrines and Their Impacts on Groundwater Quality: A Systematic Review** — Pit Latrines and Groundwater Contamination: Negative Impacts of a Popular Sanitation Method

Return to Table of Contents

Upcoming distinguished lecture features Marie Davidian

By Aleksandra Adomas

The 2012-2013 Distinguished Lecture Series will bring statistician Marie Davidian, Ph.D., to NIEHS on May 8. NIEHS Biostatistics Branch Chief Clarice Weinberg, Ph.D., will host the talk, which will explore the role of statistics in personalized medicine.

Davidian coordinates the Faculty Cluster in Personalized Medicine Discovery at NCSU, which brings together statisticians, mathematicians, and engineers to develop new methodologies for decision-making strategies in a clinical setting. (Photo courtesy of Marie Davidian)

Davidian is a William Neal Reynolds Professor in the Department of Statistics at North Carolina State University (NCSU), as well as director of the Center for Quantitative Sciences in Biomedicine. She also holds an adjunct position in the Department of Biostatistics and Bioinformatics at Duke University. Among her many honors, Davidian recently received the D.D. Mason Award, in recognition of her outstanding teaching, mentoring, and research. She is currently president of the American Statistical Association.

Discussing her upcoming talk, "The Right Treatment for the Right Patient (at the Right Time)," Davidian said the traditional tactic to evaluating treatments and approving them for the marketplace involves comparing how well they work averaged across a large number of patients. In contrast, personalized medicine takes a more targeted approach, and seeks to determine the optimal treatment for an individual patient based on all information available for that patient. This information includes not only demographic, physiological, and other clinical factors, but also genetic and genomic characteristics that could affect how the patient may respond to drugs, surgeries, vaccinations, or behavioral therapies.

In chronic diseases or disorders, such as cancer or substance abuse, Davidian said a series of treatment decisions must be made as the patient's condition evolves. The goal is to determine the most beneficial treatment option, at each stage, for patients with similar characteristics and responses to previous treatments. Statistical modeling and dynamic programming are essential to analyze the high dimensional data available for each patient, identify variables affecting the clinical outcome, and define the rules to make a personalized treatment decision. Davidian believes combining statistics and quantitative approaches with biomedical science will pave the way to personalized medicine.

(Aleksandra Adomas, Ph.D., is a research fellow in the NIEHS Laboratory of Molecular Carcinogenesis.)

Return to Table of Contents

Extramural papers of the month

By Nancy Lamontagne

Read the current Superfund Research Program Research Brief. New issues are published on the first Wednesday of each month.

Prenatal DDT exposure associated with high blood pressure in adults

NIEHS grantees report that women who experienced high levels of prenatal exposure to the pesticide dichlorodiphenyltrichloroethane (DDT) were more likely to develop hypertension as adults. Other studies have linked DDT exposure with hypertension, but the new finding suggests the association might originate in early development.

More than 40 years after the U.S. Environmental Protection Agency banned the use of DDT, the pesticide remains an important and persistent environmental exposure. In the United States, traces of DDT can still be found in some foods — primarily fatty animal products — and the pesticide is still used to control malaria in other parts of the world, including India and South Africa.

The researchers examined concentrations of p,p'-DDT and o,p'-DDT and its metabolite p,p'-DDE in blood samples collected from 527 women who were pregnant between 1959 and 1967, and part of the Child Health and Development Studies birth cohort. The researchers also surveyed the adult daughters of those women, to learn if they had developed hypertension. The investigators found that, even after adjusting for other hypertension risk factors, prenatal p,p'-DDT exposure was associated with hypertension.

Citation: La Merrill M, Cirillo PM, Terry MB, Krigbaum NY, Flom JD, Cohn BA. 2013. Prenatal exposure to the pesticide DDT and hypertension diagnosed in women before age 50: a longitudinal birth cohort study. Environ Health Perspect; doi:10.1289/ehp.1205921 [Online 12 March 2013].

Return to Table of Contents

Blocking glucocorticoid receptor prevents arsenic-induced birth defects

NIEHS grantees used computational analysis, followed by laboratory testing, to identify the glucocorticoid receptor pathway as a key mediator in metal-induced birth defects. This systems biology approach could be useful for predicting other biological pathways involved in environmentally-induced birth defects.

The researchers selected arsenic, cadmium, chromium, lead, mercury, nickel, and selenium for a computational analysis that predicted genes and pathways associated with both metal exposure and developmental defects. This analysis predicted the glucocorticoid receptor pathway was a key mediator of multiple metal-induced birth defects.

The researchers then evaluated this pathway with a whole chick embryo culture assay and an *in vitro* assay. In the chick embryo model, inhibiting the signaling of the glucocorticoid receptor pathway prevented structural malformations induced by inorganic arsenic. For the *in vitro* assay, inhibiting the glucocorticoid receptor resulted in partial to complete toxicity protection from inorganic arsenic and cadmium.

Citation: Ahir BK, Sanders AP, Rager JE, Fry RC. 2013. Systems biology and birth defects prevention: blockade of the glucocorticoid receptor prevents arsenic-induced birth defects. Environ Health Perspect 121:332–338.

Return to Table of Contents

Community beliefs regarding dioxin exposure pathways

A study, partially funded by NIEHS, found that residents of communities with known dioxin contamination made incorrect assumptions about how and where they might be exposed to dioxins. Despite the fact that dioxins aggregate, rather than disperse, in water, 79.3 percent of survey respondents incorrectly believed that dioxins could be found in river water, even after the removal of all soil and sediment. The study shows the importance of clearly communicating the specific exposure pathways of contaminants.

The researchers mailed surveys to 904 Michigan residents who lived in communities where dioxin contamination had occurred. The research team pointed out that residents have repeatedly heard that industrial discharge into the river was the source of most of the dioxin contamination. As a result, the residents concluded the river water was tainted, even though dioxins were likely to quickly bind to particles in water and accumulate in sediment at the bottom.

For future communication with residents, the researchers suggested using an analogy, such as dioxins are more like oil than water, to help mitigate concerns about drinking water and contact with river water.

Citation: Zikmund-Fisher BJ, Turkelson A, Franzblau A, Diebol JK, Allerton LA, Parker EA. 2013. The effect of misunderstanding the chemical properties of environmental contaminants on exposure beliefs: A case involving dioxins. Sci Total Environ 447:293-300.

Return to Table of Contents

BPA exposure in the NICU

A study, supported in part by NIEHS, identified medical devices as a potential source of exposure to bisphenol A (BPA), among premature infants in neonatal intensive care units. BPA is used to manufacture polycarbonate plastics, which are used in medical devices, such as intravenous administration sets, syringes, and catheters.

The researchers looked at urinary BPA concentration for 55 infants, and categorized each infant's medical device use as low or high, based on the number and invasiveness of devices. They found that the median urinary total BPA concentration of infants, who had required four or more medical devices, for three previous days, was significantly higher than for infants requiring three or less devices. The researchers also collected and analyzed breast milk or formula samples, and found that increased BPA concentration was not associated with the infants' nutritional intake.

Citation: Duty SM, Mendonca K, Hauser R, Calafat AM, Ye X, Meeker JD, Ackerman R, Cullinane J, Faller J, Ringer S. 2013. Potential sources of bisphenol A in the neonatal intensive care unit. Pediatrics 131(3):483-489.

(Nancy Lamontagne is a science writer with MDB Inc., a contractor for the NIEHS Division of Extramural Research and Training, Superfund Research Program, and Worker Education and Training Program.)

Return to Table of Contents

Intramural papers of the month

By Monica Frazier, Melissa Kerr, Mallikarjuna Metukuri, and Bailey Schug

A novel mechanism underlies glucocorticoid resistance

A recent study on glucocorticoid resistance, conducted by researchers at NIEHS, identified a novel mechanism that could have broad implications for various disorders, such as inflammation, autoimmune diseases, and cancer. Glucocorticoid resistance is caused by the repression of glucocorticoid receptor (GR) gene transcription by glucocorticoids. For the first time, they demonstrated that GR DNA sequences could act as a protein coding sequence in the absence of glucocorticoids, but repress the expression of the same gene in their presence.

Glucocorticoid resistance often affects patients undergoing long-term or high-dose glucocorticoid treatment for inflammatory disorders. Using both mouse and human cells, the authors have shown that binding of ligand-bound GR to a functional negative glucocorticoid response element (nGRE) in exon 6 enables assembly of a GR-NCoR1-histone deacetylase 3-containing repression complex. The assembly is mediated by chromatin looping of the intragenic elements at the transcriptional start site, thereby inhibiting transcriptional initiation.

The authors propose that GR and its ligand can coordinate the repression of GR transcription based on their concentration, irrespective of the combinatorial associations of tissue-specific transcription factors. Thus, their study suggests that long-term glucocorticoid administration may lead to constitutive repression of GR gene transcription and to glucocorticoid resistance. (**MM**)

Citation: Ramamoorthy S, Cidlowski JA. 2013. Ligand-induced repression of glucocorticoid receptor gene is mediated by an NCoR1 repression complex formed by long-range chromatin interactions with intragenic glucocorticoid response elements. Mol Cell Biol 33(9):1711-1722.

Return to Table of Contents

COX-2 involved in the development and worsening of asthma symptoms

NIEHS scientists have discovered that the enzyme, cyclooxygenase -2 (COX-2), is responsible for regulating a specific allergic response in persons with asthma. They found that COX-2 blocks an immune cell type that gathers around the airway when an allergic reaction occurs. The immune cell, called T helper type 9 (Th9), normally fights infection, but also releases small messenger molecules that promote inflammation, which in turn, intensifies asthmatic symptoms.

The team tested the allergic response in three sets of mice — COX-2 knockout mice, normal mice given COX-2 inhibitors, and wild-type mice with fully functional COX-2. The mice were exposed to ovalbumin, the main protein in egg whites, to generate an allergic reaction, and then the team measured the Th9 cell count. The wild type mice showed low Th9 cell counts, whereas the inhibited COX-2 mice and the mice without the COX-2 gene had significantly increased numbers of Th9 cells.

The scientists were also able to replicate their findings in humans. They determined that asthmatic patients had significantly higher numbers of circulating Th9 cells, compared to their nonasthmatic counterparts. (**MK**)

Citation: Li H, Edin ML, Bradbury JA, Graves JP, Degraff LM, Gruzdev A, Cheng J, Dackor RT, Wang PM, Bortner CD, Garantziotis S, Jetten AM, Zeldin DC. 2013. Cyclooxygenase-2 inhibits T helper cell type 9 differentiation during allergic lung inflammation via down-regulation of IL-17RB. Am J Respir Crit Care Med 187(8):812-822.

Return to Table of Contents

Early life socioeconomic factors influence the development of rheumatoid arthritis

Using data from the NIEHS Sister Study, Institute researchers have examined early life and cumulative life-course socioeconomic status (SES), and found connections with adult-onset rheumatoid arthritis (RA). This study provides additional evidence that RA may be linked with lower adult educational attainment and occupational class, and is the first to report associations of RA with younger maternal age and childhood food insecurity.

The study included 50,884 women, aged 35-74 years when they enrolled in the Sister Study, a nationwide cohort. Women were asked if a doctor had ever diagnosed them with RA, their age at diagnosis, and specific symptoms and medication use. Investigators found that several adverse childhood SES factors were more common in RA cases — young maternal age, food insecurity, and lower parental education and household income — with a significant dose-response across an increasing number of factors. This association remained in women with lower adult educational attainment and was independent from age, race, and smoking.

The findings were consistent with a cumulative effect of lower SES throughout the lifespan. Researchers suggest that these findings support further investigation of early and sustained socioeconomic adversity. (**BS**)

Citation: Parks CG, D'Aloisio AA, DeRoo LA, Huiber K, Rider LG, Miller FW, Sandler DP. 2013. Childhood socioeconomic factors and perinatal characteristics influence development of rheumatoid arthritis in adulthood. Ann Rheum Dis 72(3):350-356.

Return to Table of Contents

Specific DNA polymerase active site residue may influence a cell's mutagenic response to oxidative stress

NIEHS researches have determined the specific DNA minor groove interactions that modulate the DNA polymerase beta coding potential in response to the oxidative base lesion 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxoG). The current findings suggest the possibility to rationally design the polymerase to be less mutagenic after exposure to oxidative stress.

DNA lesions, which are created by reactive oxygen species after exposure to environmental stress, can lead to cancer-causing mutagenesis, if not repaired through base excision repair and other DNA repair pathways. 8-oxoG is considered the most abundant oxidative stress-induced lesion in DNA. When 8-oxoG is in the template base position during DNA synthesis, it can bind to DNA polymerase beta in two different conformations. This dual binding capacity leads to either a mutagenic (syn) pairing with the incoming adenine base, or non-mutagenic (anti) base pairing with the incoming cytosine base.

By introducing a point mutation into the polymerase active site that destabilizes the syn-conformation, the researchers were able to compare the specificity and kinetics of insertion with a templating 8-oxoG in the mutant and wild-type. They found the mutant DNA polymerase to be less error-prone than the wild-type enzyme, reflecting more frequent incorporation of cytosine opposite 8-oxoG.

The mutant polymerase structure, in complex with the 8-oxoG-containing template base and an incoming base, revealed that DNA minor groove interactions by the polymerase are necessary to stabilize the syn-conformation of 8-oxoG. Thus, the single active-site mutation changed the coding potential of the enzyme by modulating the 8-oxoG lesion conformation. (**MF**)

Citation: Freudenthal BD, Beard WA, Wilson SH. 2013. DNA polymerase minor groove interactions modulate mutagenic bypass of a templating 8-oxoguanine lesion. Nucleic Acids Res 41(3):1848-1858.

(Monica Frazier, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Laboratory of Molecular Genetics. Melissa Kerr studies chemistry at North Carolina Central University and is an intern in the NIEHS Office of Communications and Public Liaison. Mallikarjuna Metukuri, Ph.D., is a research fellow in the NIEHS Laboratory of Signal Transduction. Bailey Schug studies health promotion and nutrition at Appalachian State University and is an intern in the NIEHS Office of Communications and Public Liaison.)

Return to Table of Contents

Inside the Institute

NIEHS ends weeklong Earth Day celebration with local highway adoption

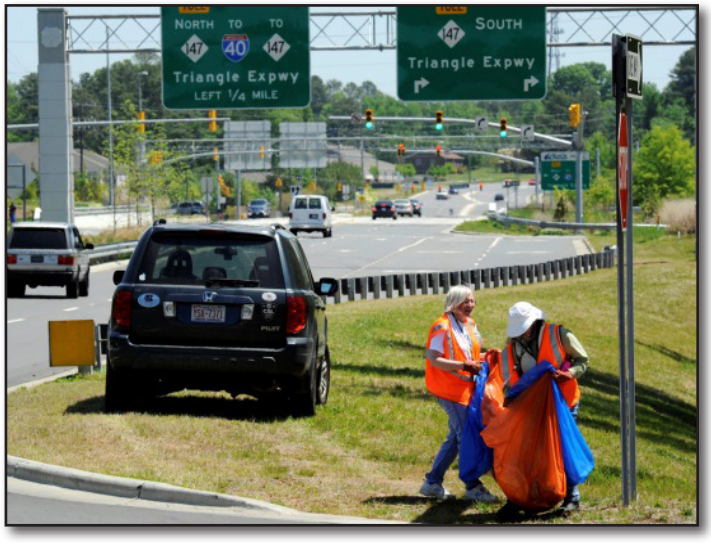
By Ian Thomas

NIEHS concluded its weeklong celebration of Earth Day April 26 by adopting the 1.2-mile stretch of Hopson Road between the main campus and Keystone building in Research Triangle Park (RTP), N.C. As part of the Adopt-A-Highway Program, the effort is intended to reduce litter on North Carolina roadsides, and help preserve the natural beauty of the state.

Adopt-A-Highway participants, from left, Paul Johnson, Bill Willis, Ian Thomas, Maggie Humble, Molly Puente, Ph.D., and Cindy Innes (Photo courtesy Steve McCaw)

"This program lets our employees take an active and immediate part in protecting our environment," said Paul Johnson, a member of the NIEHS Environmental Awareness Advisory Committee, who donned an orange vest with several of his colleagues to pick up trash. "At the same time, it also sets the example for our community that it's up to us to keep our home beautiful."

Established in 1988, as a response to growing public concerns on litter, the Adopt-A-Highway Program is managed by the North Carolina Department of Transportation, and currently hosts representatives from government and private-sector entities across the state.



Spencer, left, and Hall handled cleanup duties near the Keystone building. (Photo courtesy Steve McCaw)

A week of education

In addition to the highway adoption, NIEHS staff members were treated to a number of other educational events throughout the week. Among them was a seminar, "The effects of invasive plant species in the aquatic environment," by Rob Emens, an aquatic plant specialist with the North Carolina Department of Environment and Natural Resources (NCDENR). The hour-long talk explained how certain invasive plant species, such as Hydrilla, can have devastating ecological effects on local lakes and waterways.

"I had no idea how quickly some of these species could displace the native plants in a given ecosystem," noted Johnson. "That really underscores the sophistication of the world around us, and how interconnected everything is."

Other activities included participation in the RTP Electronics Recycling Day, and a live music and entertainment event at the U.S. Environmental Protection Agency RTP campus.

Earth Day, every day

As the week drew to a close, NIEHS and its members were reminded that, while Earth Day is only recognized once a year, its message should resonate year-round.

"Earth Day is a time to reflect on the progress we've made in protecting our environment, and to anticipate the challenges still facing us on the road to a sustainable future," said NIEHS and NTP Director Linda Birnbaum, Ph.D. "For NIEHS and its mission, therefore, every day is Earth Day."

Birnbaum applauds NIEHS efforts to increase sustainability, and promises more to come. (Photo courtesy Steve McCaw)

(Ian Thomas is a public affairs specialist with the NIEHS Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)

Return to Table of Contents

Rob Emens, from NCDENR, gave a seminar on the effects of invasive plant species in the aquatic environment, as part of the Earth Day celebration. (Photo courtesy of Rob Emens)

NIEHS Sustainability Highlights

NIEHS is a three-time U.S. Department of Health and Human Services Green Champion Award winner, for ongoing green initiatives, such as.

- Robust recycling program
- Hybrid vehicles in fleet
- Energy star-enabled IT equipment
- Cafeteria composting
- Telework for employees
- Carpools, vanpools, subsidized public transportation
- On-site shuttle
- Webcasting and greener meetings
- Reduced printing and printed materials
- Waterless urinals, low-flow showerheads/ faucets, etc.
- Occupancy sensors for lighting

NIEHS celebrates and thanks administrative staff

By Richard Sloane

Each year NIEHS holds a special event to thank the Institute's administrative staff. The annual Clerical, Administrative, Secretarial, and Technical (CAST) employee celebration took place April 22 and featured motivational speaker Earl Suttle, Ph.D. Suttle's humorous presentation held the audience totally spellbound for two hours, as he encouraged employees to be their best at work, and to find their passion, power, and purpose in life. Participants learned how to establish personal growth plans to enhance their careers.

"If you want to grow in this competitive world … build your skill security" Suttle said. "Do not do what most of the crowd does … live your life like nobody else!"

Suttle is co-author of five books, and a highly sought-after facilitator and motivator with more than 25 years of experience in team building, leadership, and personal development for corporations, universities, the National Football League, and the National Basketball Association.

"Our administrative professionals make it possible for this Institute to fulfill its research mission and to reach our scientific goals," said NIEHS and NTP Director Linda Birnbaum, Ph.D. "We appreciate them so much, and it's a lot of fun to celebrate all that they do."

Birnbaum and the rest of the NIEHS executive leadership team served ice cream cake and refreshments following Suttle's motivational seminar.

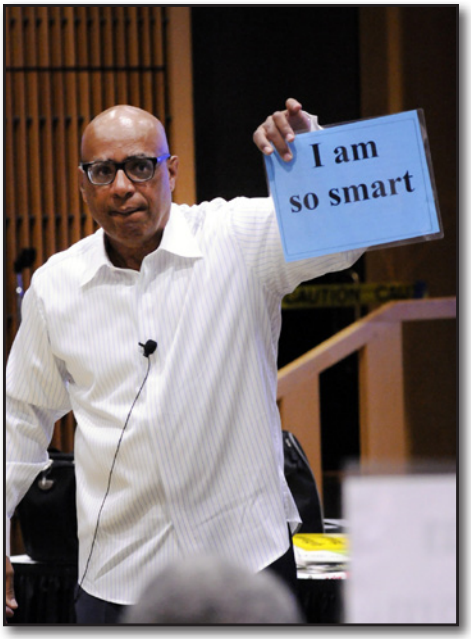
Suttle clearly loves his job and wanted to instill that same passion in the audience. (Photo courtesy of Steve McCaw)

Kathryn Woods of the NIEHS Administrative Management Branch, left, and Jennie Foushee of the Division of Intramural Research react to one of the many amusing moments during the session. (Photo courtesy of Steve McCaw)

Charletta Fowler of the NIEHS Administrative Management Branch, left, and Richard Sloane of the NIEHS Administrative Services and Administrative Branch both believed this year's CAST employee celebration was one of the best ever. (Photo courtesy of Steve McCaw)

Suttle challenges the audience to not follow the crowd. (Photo courtesy of Steve McCaw)

Kim Holmes of the Office of the Director plans to incorporate several of Suttle's practices in her work responsibilities. (Photo courtesy of Steve McCaw)



Suttle encourages audience members to think positive thoughts about themselves. Doing so will help boost their productivity and moral. (Photo courtesy of Steve McCaw)

NIEHS senior management served ice cream cake and refreshments to CAST employees. From left, Acting Clinical Director Stavros Garantziotis, M.D.; Scientific Director Darryl Zeldin, M.D.; Division of Extramural Research and Training Director Gwen Collman, Ph.D.; NIEHS Deputy Director Richard Woychik, Ph.D.; Birnbaum; National Toxicology Program Division Director John Bucher, Ph.D.; and Associate Director for Management Joellen Austin. (Photo courtesy of Steve McCaw)

(Richard Sloane is an employee services specialist with the NIEHS Office of Management.)

Return to Table of Contents

National Institute of
Environmental Health Sciences

The e-Factor, which is produced by the Office of Communications and Public Liaison, is the staff newsletter at the National Institute of Environmental Health Sciences. It is published as a communication service to NIEHS employees. We welcome your comments and suggestions. The content is not copyrighted. It can be downloaded and reprinted without permission. If you are an editor who wishes to use our material in your publication, we ask that you send us a copy for our records.

• Director of Communications: Christine Bruske Flowers

• Writer-Editor: Eddy Ball

• Science Editor: Robin Arnette